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ELECTRICAL ACTIVITY OF THE NERVOUS SYSTEM

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The subject of this article was suggested by work done recently in Cambridge on what may be called the driving mechanism of the nervous system. But my associates and I have been led to it by way of the peripheral nerves, and this account must follow the same path, starting, as anatomists would say, at the outside and working inward and upward. Such a course has much to commend it. There are many nervous reactions which can be studied most readily in the peripheral nerve fiber, although present in other parts of the neuron. One of them is the reaction with which I am concerned today, the sudden outburst of activity which is associated with a change of electrical potential.

In the nerve fiber this reaction is familiar as the nerve impulse, the brief flash of activity which spreads rapidly and is the basis of all nervous signaling. The messages which pass to and fro consist of a series of impulses in each nerve fiber, and the sole function of the fiber is to transmit them. The passage of an impulse involves a small loss of energy; the fiber must be ready at a moment's notice to react with a succession of brief explosive outbursts, and so it must maintain a store of free energy, which is replenished continually to make good the loss after each impulse. The energy level must be brought back to its proper resting value, like the water in a service tank, but the adjustments must be set so that there is no chance of a spontaneous overflow. The nerve fiber must act as an indifferent conductor, transmitting an impulse only when one is sent into it from a sense organ or a nerve cell.

The sensory ending has a less stable make-up. It has to signal the occurrence of a slight change in its environment, e. g., a mechanical strain, and the only way in which it can do so is by sending a series of impulses up the fiber. A slight deformation of its surface will start a rhythmic beat, a repeated breakdown and repair continuing in many types of ending as long as the disturbing factor is present. This factor has altered the adjustments of the tank, the water levels and the syphoning arrangements, so that it fills up and empties repeat-

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edly. All records of the action potentials in a sensory nerve trunk tell the same story. They show the nerve fiber and the sensory ending as structures which liberate stored energy in a succession of jerks, the intensity of the stimulus being signaled by the frequency of the outbursts. It is probable that this mode of working is essential in any living system concerned in rapid long-distance signaling and operating, as in the neuron, by the spread of a surface change. It involves the continual replenishing of the energy level in the system and some kind of trigger mechanism to control the discharge.

It is obviously a very small step from a system like the sensory ending, which beats as long as it is under slight tension, to one which beats continually. A good many sense organs do so normally, for many of them give a slow resting discharge which ceases for only a few moments after prolonged stimulation. Again, a change in the saline environment (e. g., the presence of citrate of oxalate) will make a tactile ending discharge continually at a high frequency for hours on end. It would not be difficult to arrange a mechanical model which could be made by a slight change of adjustment to react like the nerve fiber, which needs a separate stimulus for each beat, like the sense organ which beats rhythmically as long as the stimulus persists, or like the heart, which beats as long as it is alive. But one can do better with a physiologic model. A fiber of the frog's sartorius muscle is normally under the control of the central nervous system and responds only when an impulse is sent into it; but if it is bathed in a solution without calcium it first shows a stage in which a mechanical stimulus will produce a succession of beats and eventually beats continuously. During the intermediate stage the muscle fiber makes a crude copy of a sense organ and in the final stage it has become like the heart.

Behavior like that of the heart muscle, the system adjusted for repeated spontaneous discharge, is, and must be, abnormal for most of the executive apparatus of the body. The motor neurons and the skeletal muscles must be under the complete control of the central nervous system and must remain at rest when they are not activated by the higher centers. In the higher centers, however, this behavior would not be so intolerable. As will be seen, there are cell mechanisms in the brain which are set so that a periodic discharge is bound to take place. The moment at which it occurs can be greatly altered by afferent influences, but it cannot be postponed indefinitely.

The most obvious instance of this in the mammal is to be found in the respiratory center. Winterstein's experiment showed that the center continues to discharge periodically although there is no corresponding afferent rhythm to drive it and although in the intact animal the rhythm is greatly modified by impulses from the vagus and elsewhere. The rhythmic movements of "narcosis progression" studied by Graham Brown and those of Amblystoma larvae (Coghill) are probably determined

by a spontaneous overflow of the same kind. These examples are well known because the nerve cell rhythms are made evident by corresponding movements of the body. For most of the brain, however, there is no direct path to the muscles. One can ascertain what the cells are doing only by recording the changes which are taking place in them; and the only changes which one can study in a nerve cell without interfering with it are the changes of electrical potential which accompany each period of activity. This brings me to the main problem—the nature of the electrical changes which can be detected in the cortex and the conditions which give rise to them, or rather to the cortical activity which they represent.

The electrical changes in the brain have been studied in a number of laboratories from various aspects. The present account must be confined to one aspect and must avoid the technical details. A record (fig. 1) made from the cortex of a rabbit under chloralose anesthesia will show what one has to deal with. It consists of large irregular potential waves, of various shapes and sizes, and of small rapid waves as well. The

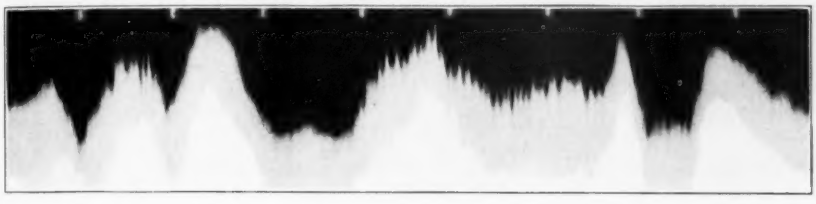

Fig. 1.—Changes in potential from the exposed cortex of a rabbit under chloralose anesthesia. The time marker gives one-fourth second intervals.

large, slow waves are summation effects due to repeated pulsations occurring out of phase with one another in many neurons. They show when the total activity becomes more intense, but do not show what it is like in each neuron. The activity is, in fact, much like that of the nerve fiber, a rhythmic series of outbursts, less abrupt than the nerve impulse but having much the same range of frequencies. To produce the large deflections by a summation of the outbursts in each neuron there must be some agreement in the periods of rest and activity over large areas, but in the lightly anesthetized animal, and still more in the unanesthetized animal, the activity may be extremely irregular, varying from point to point and from moment to moment. Simultaneous records from several points show the patterns of activity in the cortex, and, as one might expect, these patterns shift rapidly under the play of afferent stimuli.

What happens to this electrical activity when the animal is more deeply anesthetized? One would guess that it would stop entirely, but instead of this it often becomes much more regular. Under light chloroform anesthesia a regular series of waves at from 3 to 4 a

second usually appears in the rabbit's cortex (fig. 2 *A*). This rhythm may be confined to a restricted area, but in deep anesthesia the periods of activity occur at longer intervals (about one every second) and the whole cortex beats with this rhythm (fig. 2 *B*). This regular alternation of periods of rest and periods of activity takes place at a stage of anesthesia so deep that no message can reach the cortex from the sense organs and no efferent messages can be sent to the muscles. At such a stage it is remarkable to find any cortical activity, and still more remarkable to find that it is not a random activity of isolated units but a wave which spreads throughout the cortex as if it were so much heart muscle. But the neurons of the respiratory center are still giving their periodic discharge; one has only to suppose that the cortical cells (or possibly the cells in some subcortical center which is closely connected to the cortex) have the same tendency to beat spontaneously when they are left alone. The anesthesia seems to have isolated them from

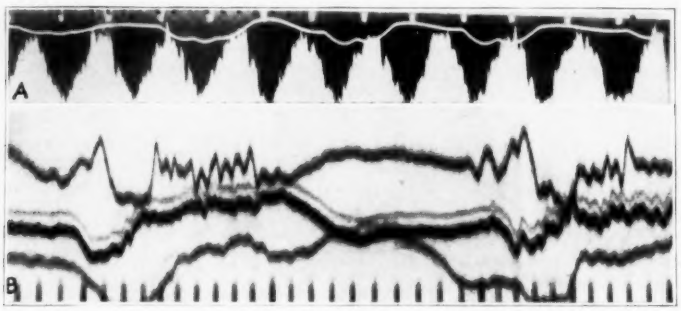

Fig. 2.—*A* shows regular potential waves from the cortex of a rabbit under light chloroform anesthesia. The white line signals respiration. The time marker gives one-fourth second intervals. *B* shows slow periodic activity of the cortex with the rabbit under deep chloroform anesthesia. Records from three pairs of electrodes show the coincidence of active periods at different points. The time marker shows one-twentieth second intervals (for details see Adrian and Matthews: *J. Physiol.* **81**:440, 1934).

the rest of the nervous system but not from one another. By doing so it enables them to show their spontaneous rhythm, and they can beat together because they are no longer exposed to the usual mosaic of afferent influences. This tendency to synchronous action is not peculiar to the cortex, for there are other groups of nerve cells which come to act in unison if they are exposed to uniform conditions of excitation or of lack of excitation. And the break-up of the collective action can be seen clearly when one uses lighter anesthesia and disturbs the cortex by a sensory message. This abolishes the large waves and substitutes a rapid, irregular oscillation of much smaller amplitude (fig. 3). The extinction of the large waves gives the impression of a falling off in activity, but it must be remembered that persistent activity, if not

synchronous, would give rise to nothing more than small rapid oscillations of the kind shown in the latter part of the record. The failure of the large waves merely shows that the collective beat has ceased.

These records suggest that many of the cerebral neurons are so constituted that they must discharge periodically, like the cells of the respiratory center. In normal conditions they will be controlled, like the respiratory center, by afferent messages, but if they are undisturbed they will beat with their proper rhythm and will tend to beat in unison. But the records are from anesthetized animals, and it has been assumed that the anesthesia merely allows the rhythms to develop by cutting off disturbing influences. What evidence is there to show that it has not a much more direct effect, that it has not changed the adjustments of the nerve cells as a sodium chloride solution changes the adjustment of a muscle fiber? There is no direct evidence, but there is distinct support from an unexpected quarter, from the brain of normal, unanesthetized man.

During the past five years, Hans Berger,[1] of Jena, has published a series of papers describing the human "electrencephalogram"—the

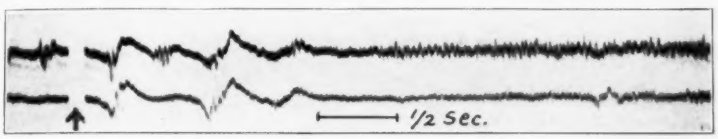

Fig. 3.—Record from the cortex of a rabbit under ethyl carbamate (urethane) anesthesia, showing large waves abolished by sensory stimulation. The arrow marks the moment at which the foot was pinched. The short horizontal line indicates one-half second.

electric oscillations led off from the head and due, he believes, to action potentials in the brain. He records them by needle electrodes piercing the scalp. He found a regular series of waves at a frequency of 10 a second when the subject lay on a couch with his eyes closed. These waves disappeared when the eyes were opened or when the attention was fully occupied. Matthews and I have repeated many of Berger's observations. We have had no difficulty in finding the rhythm that he described, and after an initial period of skepticism we have come to believe in its cortical origin.

Any one familiar with electrical technic will understand our hesitation on this point, in spite of the well planned control determinations, reports of which Berger has published. The head contains many possible sources of potential change apart from the brain, mechanical artefacts, action currents from muscles in the scalp, face or neck, changes due to movements of the eye, etc. For a time we thought that eye move-

1. Berger, H.: J. f. Psychol. u. Neurol. **40**:100, 1929; Arch. f. Psychiat. **94**:16, 1931; **97**:6, 1932; **98**:231, 1932; **99**:555, 1933; **100**:307, 1933.

ments were responsible, but in the end we have had to agree that the rhythm is due to the cortex. On one point, however, we seem to differ from Berger, for we believe that the waves arise from the occipital part of the brain, from a region intimately connected with the visual centers, whereas Berger, if we have understood him correctly, gives them a wider and less specific origin.

Typical records of the waves are given in figure 4. They are made, as in all our experiments, by leading off from the intact scalp with moist pads, one just above the occipital protuberance and one on the vertex. We find that the waves are always greatest when one lead is on the occiput, though in normal subjects they can be detected much farther forward. In subjects whose skulls have been trephined laterally, the localization to the occipital region is sharper, the opening in the skull giving a pathway of low resistance to the brain.

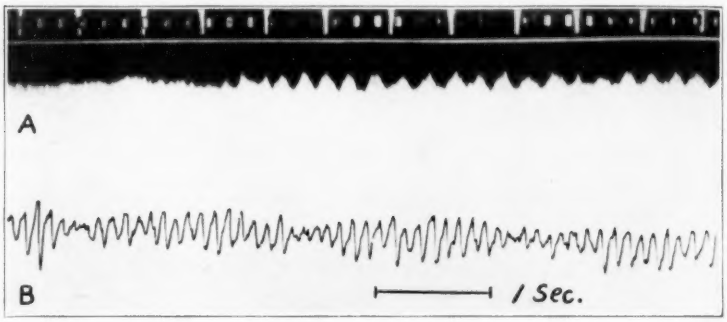

Fig. 4.—Rhythmic potential waves, as described by Berger, recorded with electrodes on the scalp at the vertex and the occiput. *A* (record for E. D. A.) shows the development of rhythm on closing the eyes. In *B* (record for W. H.) the eyes were closed throughout (Matthews ink writer oscillograph).

The subjects from whom these records were made were sitting with closed eyes, for the chief condition for the appearance of the waves is that there shall be no visual activity. The closure of the eyes is not essential; but it is essential that visual attention should not be aroused either actively or passively. For instance, if the head is enclosed in a dark box, the waves will appear with the eyes wide open, but not until the subject has ceased trying to see anything. The visual field may be moderately light or quite dark, but it must be so uniform that it contains nothing to attract the attention (fig. 5).

Provided the eyes are shut, a considerable amount of mental and bodily activity can go on without interfering with the rhythm. The subject can enter into a conversation, squeeze a dynamometer or stick a pin into his finger with at most some reduction in the amplitude of the waves. But they are abolished, as Berger has shown, by anything which engages the subject's full attention. The working out of a diffi-

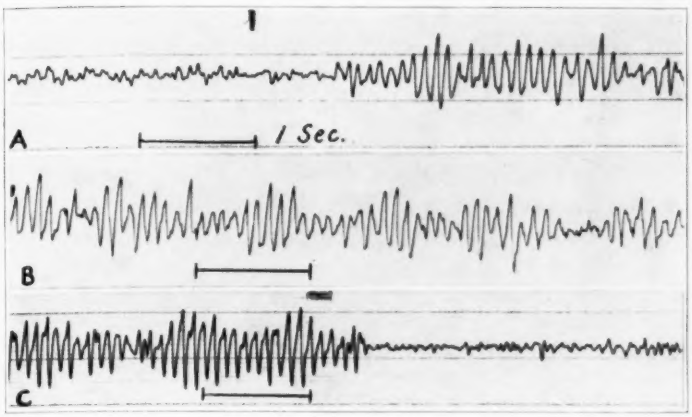

Fig. 5.—Records showing dependence of rhythm on absence of visual activity: *A*, for L., with the eyes closed at the signal; *B*, for A., with the head in a dark box and the eyes open, and *C*, for Y., with the eyes opened at the signal.

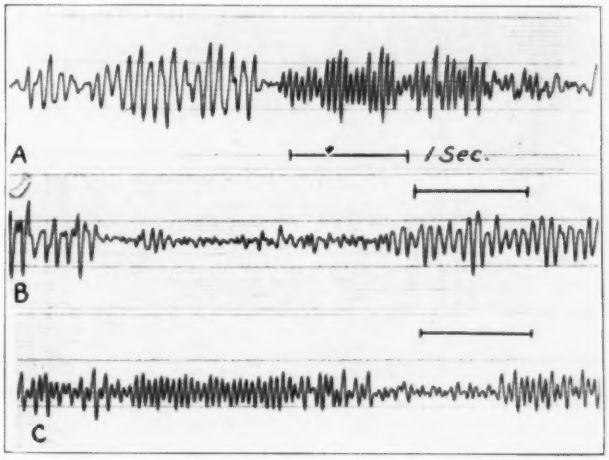

Fig. 6.—Records illustrating rhythms induced by a flickering field. The eyes were close to the concave surface of an opal glass bowl lighted by a beam interrupted by a sector wheel. *A* shows record for E. D. A. with flicker at 20 a second and the eyes opened half-way through the experiment. Ten a second rhythm changes to 20 a second. *B* shows a record for Y. with flicker at 13 a second and the eyes opened near the beginning of the experiment. Rhythm at 13 a second develops at the end. *C* shows a record for Y. with flicker at 18 a second and the eyes open throughout. There is occasional half rhythm. The short horizontal line marks one second.

cult problem in mental arithmetic, an attempt to hear a watch ticking at the maximum distance or a pinprick administered unexpectedly by some one else will annul the rhythm for the time being. The difference is that a very mild degree of visual activity will abolish the waves, whereas nonvisual activity will not do so unless it occupies the whole mind.

It is important to note that these activities do not change the rhythm. The waves may continue with diminished amplitude or may give place to small, irregular oscillations, but as long as there is any rhythm its frequency remains unaltered at a value which is very close to 10 a second in every subject. The rhythm can be changed, however, and in a way which emphasizes its close connection with vision—if the eyes are exposed to a flickering field of large area the potential waves take on the frequency of the flicker. Records showing this effect are given in figure 6. The normal 10 a second waves and those produced by the flicker arise from the same region of the brain or from closely adjacent regions, for they show parallel variations in size when the electrodes are shifted. The rhythm of the flicker is followed up to rates of 25 a second (higher rates have not been tested), but with very low rates there is a tendency to revert to the 10 a second rhythm. By adjusting the rate of flicker to coincide exactly with the natural rhythm it is possible to obtain an exceedingly regular series of waves.

COMMENT AND SUMMARY

These facts may be summarized as follows:

1. There is an area in the occipital region of the human brain which can produce rhythmic changes of potential large enough to be detected through the skull when the subject looks at a flickering field.

2. When there is no visual activity the area gives rise to waves of the same order of magnitude with a fixed rhythm of 10 a second.

3. This rhythm is abolished by visual stimuli of the customary irregular type, and by nonvisual activities which claim the whole attention.

That rhythmic changes of potential can be induced by flicker is not surprising. With the whole field flickering and a million or more optic nerve fibers sending the rhythm to the brain, one would expect that the striate area and probably a great deal of the neighboring cortex would be forced to beat at the same rate. Owing to its position the striate area would be unlikely to contribute much to the changes in potential led off from the head, and it is probable that the cortex on the lateral aspects of the occipital lobes is responsible for them. To account for the appearance of a constant rhythm when this area is left to itself, one has only to turn to the records of potential from the rabbit's cortex. In these there is evidence of large groups of neurons beating spontaneously

when they are cut off from the disturbing effect of afferent messages. And one would expect this spontaneous rhythm to fail when the subject looks at a steady, nonuniform field, for the mosaic of excitations would make it impossible for the different neurons to keep up a synchronous beat. In fact, a record from a human being with the eyes first closed and then open is in every way comparable with one from the rabbit's cortex when the foot is pinched (fig. 7).

We assume, therefore, that the phenomenon, which may be suitably named the Berger rhythm, represents the spontaneous beating of a part of the occipital lobe. The neurons in this region tend to discharge periodically when they are undisturbed and to work in phase with one another when there is nothing to prevent them. The synchronous beat is disorganized most readily by visual activity, but the area is accessible to the rest of the brain and is invaded by any kind of activity which demands complete attention.

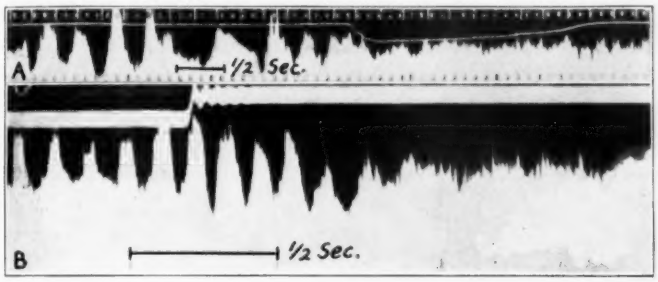

Fig. 7.—*A* shows the record from the exposed cortex of a rabbit under ethyl carbamate (urethane) anesthesia. There is abolition of large waves on sensory stimulation (foot pinched at signal). *B* shows the record from a man (E. D. A.) with electrodes on the scalp at the vertex and the occiput. The Berger rhythm is abolished by opening the eyes. The short horizontal line indicates one-half second.

It is probable that the cortical neurons in general have this tendency to rhythmic beating but that the only regions likely to give a measurable effect through the skull are those normally occupied with vision. By closing the eyes the largest inflow of afferent messages to the brain can be cut off, leaving a large area of the cortex with nothing to do, and there is no other sense which plays so great a part in cortical activity and is so readily controlled.

It is interesting to find that the area is compelled to give up its synchronous beat when the subject's whole attention is claimed by a problem in mental arithmetic or by an unexpected pinprick. Widespread bodily activity often accompanies the mental effort or the emotional shock, and presumably the widespread cortical activity reaches the occipital region. But the visual pathway has the first call on it. The forced rhythm due to flicker persists unchanged in spite of mental

effort. Again, as one might expect, a flickering field can impose its rhythm even though the subject concentrates his attention on a fixation mark in the center. Provided the flicker covers most of the visual field the pulsation will appear, although the activity is not uniform in all parts of the area. On the other hand, if all visual activity has been in abeyance for a long period the area seems to acquire a closer connection with other parts of the brain and to be more easily affected by nonvisual activities. That, at least, would explain our failure to find the Berger rhythm in patients who have been blind for some years.

I have stated our conclusions with little detailed evidence and no mention of the tedious but all-important subject of controls. And I have said far too little about Berger's own extensive work and of the conclusions that he has drawn. I can only plead that the time is lacking and that any problem of cortical function can be viewed from so many angles that one must keep to one's own standpoint or abandon all sense of direction. The view put forward—of brain cells tending to beat spontaneously in groups—has little direct bearing on most of the questions debated by neurologists. In spite of its academic character one may hesitate to accept it, arguing that differences in potential of a tenth of a millivolt between two points on the scalp are a slender basis for any theory of cortical activity. But the theory has at least the claim to consideration that it is a convenient peg on which to assemble the facts and that some of these are interesting in themselves.

DISCUSSION

Dr. Walter Timme, New York: Might not the effect of the opening and closing of the eye be due to the change in the size of the pupil rather than to the element of vision, the change in the size of the pupil being correlated via the sympathetic nervous system with a change in the blood vessels of the occiput? These vessels are controlled by the cerebrosympathetic nervous system; might they not, therefore, produce this change of rhythm?

Dr. E. D. Adrian, Cambridge, England: I do not think that the rhythm itself could depend on a rhythmic stimulation or rhythmic movement of the pupil producing an oscillating vascular reaction. The rate may be as high as 20 a second with a flickering light, and it is unlikely that there could be vascular changes at such a high frequency. But some reflex vascular change might start and stop the 10 a second rhythm. I do not think that we have ever had that possibility in mind. It is certainly worth considering.

Dr. Donald J. McPherson, Boston: Has Dr. Adrian tried making visual images, and if so, could the images derived from an imaginary source have an effect like that produced by allowing images to come in through the eye?

Dr. E. D. Adrian, Cambridge, England: No. We have tried to abolish the rhythm by visual imagery, but neither Matthews nor I can do so. The mind's eye, so to speak, is not concerned in the effect. The phenomenon seems to be very much on the material plane.

DR. TRACY G. PUTNAM, Boston: Is it true that these electrical effects can be taken off only from the occipital region and that the other portions of the surface of the cranium do not yield similar results?

DR. E. D. ADRIAN, Cambridge, England: When the skull is intact the electrical effects can be led off from any part of the scalp, but they are definitely larger when one of the leads is on the occiput. The skull forms a layer of high resistance surrounding the brain and makes sharp localization impossible. But an opening in the skull makes a pathway of low resistance to the brain. With one lead over a trephine opening and another in front there is usually no sign of the rhythm, although it becomes clear if the front lead is transferred to the occiput. This is good evidence of an origin from the occipital region of the brain, but I cannot say how large an area is involved.

DR. ERNST A. SPIEGEL, Philadelphia: Has Professor Adrian any theory as to why the period of latency is so long, apparently nearly one-half second?

DR. E. D. ADRIAN, Cambridge, England: All that can be said is that the rhythm is probably due not to the striate area itself but to a neighboring part of the cortex. The period of latency may represent the time taken for the effect to spread from the striate area, but in any case a synchronous pulsation might take some time to become fully established.

QUESTION: What is Professor Adrian's attitude in regard to the work of the institutes in Berlin? Fischer and Kornmuller have found that areas in the brain differing in cyto-architecture give characteristic electric effects. Furthermore, they claim that the application of optical stimuli on the retina gives a persistent change of potential in the striate area.

DR. E. D. ADRIAN, Cambridge, England: I do not think that there is any real conflict between the results of Fischer and Kornmuller and those of Berger and ourselves. Fischer and Kornmuller have recorded the potentials in the striate area when the eye is illuminated, and they have noted the "on-and-off" effect which one might expect from this area. It is true that there is no sign of a rhythm at 10 a second in most of their records made with the eyes in darkness, but in rabbits and cats the visual centers are less highly developed than in man and there may be nothing to correspond to the area which gives the rhythm in man. If we assume that this is not the striate area, the results obtained in animals and those observed in man are not contradictory.

I cannot say that our results lend much support to Kornmuller's view that there are specific types of electrical change corresponding to areas of different cyto-architecture. This may be so, but in subjects under light anesthesia there is so much variation from time to time that it would be hard to recognize a specific type of response. However, we have not worked under the same conditions and have not made any special investigation of the point.

DR. WILDER PENFIELD, Montreal, Canada: Professor Adrian's demonstration of nervous control of respiration has brought a great deal of satisfaction to one neurologist whom we all venerate. I had an opportunity to visit Sir Henry Head a little over a year ago. He had just been visited by Professor Adrian, who was returning from the congress in Rome. Professor Adrian had brought with him a phonograph disk which recorded in an auditory way the impulses which he has just shown in one of these slides, impulses from the diaphragm indicating and proving definitely the nervous control of respiration.

During the years following Head's original demonstration of nervous control, the fog, if I may call it that, of chemical work almost obscured the neurogenic mechanism. Head played this record over twice to me, and it is reasonable to believe that this belated verification is welcome music in his ears.

Dr. J. G. Dusser de Barenne, New Haven, Conn.: It may be interesting to mention in this connection that if one leads from the motor cortex in the monkey (and in other animals), one gets, as is known, very irregular spontaneous action currents, but if the three superficial layers are destroyed and only the two inner cell layers are left behind (by laminar thermocoagulation) there often occurs a slow, regular rhythm of about 10 to 12 waves per minute—large potential waves.

RELATION OF THE CONDITIONED REFLEX TO PSYCHOANALYTIC TECHNIC

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In recent years several efforts have been made to work out the relationship between psychoanalysis and the experimental studies of the conditioned reflex. Outstanding among these have been the studies of French,[1] and Ischlondsky,[2] in which psychoanalytic theory and the experimental findings of Pavlov have been correlated. The present study, however, is confined to an investigation of the relationship of the conditioned reflex to psychoanalytic technic for the purpose of showing that psychoanalysis, as a method of fact gathering, has a sound basis in accepted physiologic laws.

The point of departure is found in a quotation from Pavlov[3]:

> The process of synthesis—that is, of association—may take place in a state of inhibition on account of the existence at the moment of a predominant focus of strong excitation. Although the actual synthesizing activity may not enter our field of consciousness, the synthesis may nevertheless take place, and under favorable conditions it may enter the field of consciousness as a link already formed, seeming to originate spontaneously.

Pavlov stated further that this experimental fact must throw light on the relationship of the conscious to the unconscious. Although the quotation is from Pavlov, it sounds as though it might have been culled from the pages of Freud. It summarizes an experimental demonstration of one of Breuer and Freud's earliest psychoanalytic observations: to wit, the fact that a focus of strong excitation can give rise to a generalized inhibition, and that under such circumstances important, unconscious chains of associative connections can be set up in the inhibited field. Of special significance, however, to the problem of technic is the statement that "under favorable conditions, the unconscious synthesis may enter the field of consciousness." What are the "favorable circum-

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Read before the New York Academy of Medicine, Section of Neurology and Psychiatry, Dec. 13, 1932.

1. French, T. N.: Interrelations Between Psychoanalysis and the Experimental Work of Pavlov, Am. J. Psychiat. **12**:11 (May) 1933.

2. Ischlondsky, N. E.: Neuropsyche und Hirnrinde: Band II. Physiologische Grundlagen der Tiefenpsychologie unter besonderer Berücksichtigung der Psychoanalyse, Berlin, Urban & Schwarzenberg, 1930; Der bedingte Reflex und seine Bedeutung in der Biologie, Medizin, Psychologie und Pädagogik, ibid., vol. 1.

3. Pavlov, I. P.: Conditioned Reflexes: An Investigation of the Physiological Activity of the Cerebral Cortex, translated by G. V. Anrep, New York, Oxford University Press, 1927.

stances" to which Pavlov referred that will allow unconscious associations to escape from the inhibited or unconscious field and enter the field of consciousness? And does the psychoanalytic method facilitate this emergence from inhibition?

In order to answer this question one must understand what Pavlov meant by conditioned excitation and conditioned inhibition. The process of cerebral excitation by a positive conditioned stimulus will be considered first. The conditioned stimulus is always a signal. When it is excitatory in its action it is a signal to the animal that something is to follow. Moreover, the "something which is to follow" must have a definite emotional and instinctual significance to the subject of the experiment. It is for this reason that the effect of the stimulus depends not only on its own intensity but on the state of instinctual tension in the animal or the human subject at the moment of stimulation. Furthermore, although time intervals may be varied, the sequence of events can never be reversed. The conditioned stimulus must always come first, to act as the signal that a gratification is coming, if it is to have any excitatory effect on the cortex. The action of an excitatory conditioned stimulus may be summarized as follows: The animal must be in a state of instinctual craving and not of satiety, and the stimulus must regularly precede the gratification and thus become a signal of its approach.

It must be borne in mind, however, that even an effective excitatory stimulus exerts two kinds of inhibitory action on cortical functions. In the first place, it inhibits the activity of the cortex in the areas which are not involved directly in the process of excitation and response. In the second place, during the period of lag between the stimulus and the response there is active inhibition operating over the entire cortical field. Inhibition appears, therefore, in the train even of active excitatory agents.

There is, furthermore, another form of inhibition which is of importance in its implications to analytic technic. This is the action of such conditioned stimuli as signal to the animal the fact that nothing, literally nothing, is going to happen, whether of an instinctually gratifying or of an instinctually threatening nature. It is one of the most distinctive achievements of Pavlov and his co-workers to have demonstrated that a stimulus which signals to an expectant animal that nothing of consequence is going to happen to it exerts an inhibitory action on cerebral function, first in a scattered and patchy way and finally in an all-pervading fashion that leads to sleep. (This is why the patient who is actively, even though unconsciously, craving some form of gratification from the analyst, and who is frustrated by the analyst's quiet unresponsiveness, so regularly complains not of his frustration but of sleepiness.)

Thus, the cerebral cortex is constantly being stimulated, not only toward activity but also in the direction of inhibition. This inhibition

may be diffuse, pervading the entire cerebral function, or its areas of influence may be circumscribed and patchy. It may arise in the train of stimuli which are excitatory in their direct effects, or may result from specifically inhibiting conditioned stimuli. All stimuli, therefore, whatever their nature, are constantly creating zones of partial, circumscribed or diffused inhibition; and particularly every stimulus which evokes no effective response acquires with repetition an inhibitory value, with a consequent tendency toward the extinction of all unreenforced reflexes. One might phrase the formula as follows: Excitation plus no response equals inhibition.

It must be obvious, therefore, that when one desires to study spontaneous cortical functions it is necessary to reduce to a minimum the mass of stimuli which are impinging on the central nervous system. It is only by doing so that one can create in the cortex an equipotential field, i. e., one in which all units have an equal chance of coming into active expression. Otherwise, the accumulated inhibitory effects will distort the very data which one is aiming to investigate. It is for this fundamental physiologic reason that the analyst who wishes to lift some of the blanketing inhibitions which obscure so much cortical synthesis must play an extraordinarily passive rôle. Like the unseen observer of the experimental animal in a laboratory for the study of the conditioned reflex itself, he must be quiet, impersonal and at least relatively invisible to the patient. For reasons which will be given later, he must offer as few emotional gratifications as possible. The full implications of this are somewhat astounding and, superficially regarded, appear paradoxical. It seems absurd to say that the more "stimulating" the physician is, the more he blankets the patient's own cortical productions under strong inhibition, and that the more passive and subdued he is, the more he releases the patient's cortical productions. Yet that seems to be an inescapable conclusion from Pavlov's work, and one which coincides closely with actual analytic experience. (For the sake of clarity, it may be worth while to add the obvious comment that from time to time for special reasons the analyst and the experimenter both leave off their cloaks of invisibility and play for a few minutes a more active rôle. When this is done, however, it is with a clear and special purpose, which in no way alters the fundamental principle which has been discussed.)

It is fair to claim, therefore, that the psychoanalytic procedure reduces to a minimum that form of inhibition which Pavlov has called "external inhibition." In so doing it reverses the inhibiting action of the "predominant focus of strong excitation" to which Pavlov referred in the foregoing quotation.

With the lifting of this blanketing inhibition it becomes possible for the analyst to explore the inhibited field by means of the method of free association in which the free associations of the patient are

both stimulus and response. One must bear in mind that the chief response which is recorded in the dog is an automatic secretory reflex of which the animal is himself unaware and to which he has no means of responding. The patient, on the other hand, responds with speech, gestures and facial expressions, or with bodily sensations and emotions. Because the analyst reduces external stimuli to a minimum, in the process of free association each one of these responses becomes in turn the stimulus for new responses, new speech and new feelings. Each reaction thus becomes a link in a chain of conditioned stimuli, conditioned responses and conditioned inhibitions. As Pavlov showed, there is an intricate mosaic of conditioned reflexes, one interrelated with another, and all of them interweaving in and out of the fields of excitation and inhibition. It becomes inevitable, therefore, that as the analyst follows along this chain of conditioned reflexes which are called spontaneous free associations, he too moves with the patient in and out of the field of conscious and unconscious synthesis. It is by the use of each response as a stimulus to a fresh response, in the absence of external inhibition, that the patient is inevitably led through the inhibited or unconscious field.

This brings up another fundamental consideration. The outstanding fact about the conditioned reflex is that the conditioned stimulus is related to the unconditioned stimulus for one reason only, namely, that the two exerted their influence on the central nervous system in a certain definite time relationship. Any alteration in that time relationship would have changed their internal connections, and could even change an excitatory into an inhibitory agent, or the reverse. Time relationships, therefore, are the most fundamental of all facts in the interrelating of experiences by the central nervous system.

As a result, the analyst is justified in making the tacit assumption that whenever two ideas appear in a patient's mind in a definite sequence or relationship to time, even if there is no superficially discernible logical relationship between these ideas, the mere fact that they have appeared together is evidence that there must be some dynamic relationship between them in this particular person. It may be said that this premise is the mirror image of the experimental fact on which the whole structure of Pavlov's work rests, for it is perhaps the chief contribution of the Russian school to have demonstrated that the cerebral functions do not operate on a basis of logic alone, but that accidental intervals and sequences in time exert a determining influence on the patterns of association and on the excitatory or inhibitory effects of events. Without at first fully realizing how well grounded is its basic method, psychoanalysts have made fruitful use of this observation. They have realized that the patient whose exploration of his psyche is limited by the tyranny of logic remains only in well worn paths and learns nothing of that vast

area of cerebral syntheses which lies off the beaten paths of conscious logical thought. The analyst has learned, furthermore, that if the patient is helped to travel along the unguided pathways of free association, allowing each mental product to serve as a conditioned stimulus for the next and using no other guide in his interpretation of these sequences than their proximity in time, there gradually unfolds a picture of the interrelation of the fields of conscious and unconscious thought, or, in the Pavlovian terminology, of excitation and inhibition.

In one final consideration, however, the psychoanalyst is forced in part to disagree with Pavlov. At the beginning of his work, Pavlov, with his deep antipathy to orthodox psychology, attempted to identify instinct and the conditioned reflex. This identification must be questioned not on psychoanalytic grounds alone, but also on those of common sense; however, it is fair to say that with increasing clarity as his work developed Pavlov gradually recognized important differences between these two phenomena. He saw that there was an obvious difference of great importance between the physiologic system of the knee jerk (in which all of the energy is supplied by the blow and by the peripheral neuromuscular apparatus) and such a system as that of the conditioned reflex, which depends on energy which has been stored within the central apparatus. Furthermore, Pavlov came to realize the important significance of the amount of instinctual tension under which the animal labored. Thus he found that there were evident differences between the response of a hungry dog and that of a satiated dog, or between the response of a dog when "nervous excitability" had been increased by caffeine and that of one which had been given bromides, with, respectively, a resulting loss or increase of inhibitory phenomena. Indeed, he found that in the absence of instinctual tension no conditioned reflex could be established, and that with complete satiety both the conditioned and the unconditioned reflex became completely inhibited. The reservoir of energy, therefore, on which the entire phenomenon rests is the instinctual energy, which in analytic terminology is spoken of as the libido. In this observation there is for the analyst an important practical implication. To the extent to which the analyst or the physician pacifies, placates, mollifies or reassures or in any other way gratifies the patient, to that extent he spreads the blanketing action of inhibition over the cortical field. And in so doing he defeats his own inquiries into the unconscious syntheses. The analyst is forced, therefore, to maintain rigorously his attitude of stern and unrewarding aloofness, rarely allowing his emotional gratification of the patient to go beyond that attitude which Jones has called so aptly one of "benevolent curiosity." It is only in this way that the patient's instinctual demands can be mobilized in the service of the investigation of his cortical functions.

One is forced, therefore, to the conclusion that the passive observer who restrains his natural curiosity and asks few or no questions, who avoids all external stimulation of the patient, who strives at every point merely to facilitate the patient's free flow of unguided and undirected speech—that is, his production of speech in which each element acts as the conditioning stimulus of the next—is actually presenting a spoken version of a classic experiment on the conditioned reflex. He is reducing the inhibitory influences to a minimum, and thereby allowing those unconscious syntheses which Pavlov pointed out as occurring under inhibition to emerge into the field of consciousness. He is depending on the fundamental temporal sequences to reveal these connections, rather than forcing them into arbitrary rationalistic systems. He works on the premise that any two ideas which emerge from the patient together or with any characteristic sequence must by virtue of that fact alone have some dynamic relationship in that particular person's psychology; and this premise rests squarely on a legitimate deduction from sound experimental observations.

COLLOIDAL THORIUM DIOXIDE

ITS USE IN INTRACRANIAL DIAGNOSIS AND ITS FATE ON DIRECT INJECTION INTO THE BRAIN AND THE VENTRICLES

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Visualization of intracranial structures is of value in localization and general neurologic diagnosis. In addition to ventriculography with air (Dandy), the visualization of various structures by the injection of colloidal thorium dioxide (thorotrast) into the subarachnoid space has recently been reported. By the lumbar or suboccipital injection of from 5 to 8 cc. of colloidal thorium dioxide Radovici and Meller [1] and Wustmann [2] have shown the surface outlines of the brain, some of the cranial nerves, the brain stem and the spinal cord (encephalography and perieencephalomyelography). This procedure is reported to have good possibilities. It is recommended that as soon as roentgenograms have been taken, the patient be put in the upright position and that spinal fluid be withdrawn by lumbar puncture; an appreciable amount of colloidal thorium dioxide can thus be removed from the body. Wustmann pointed out that when colloidal thorium dioxide is used in this way a buffered preparation should be used; this is well tolerated, while the use of the older preparation, which is not buffered, is often followed by serious symptoms. This procedure has not yet been carried out in this clinic.

The second use of colloidal thorium dioxide in the diagnosis of intracranial lesions is the visualization of cerebral arteries. From 8 to 12 cc. of the substance is injected into a carotid artery, and a roentgenogram of the head is taken just as the injection is being completed. A number of favorable reports on this procedure have been made, namely, by Egas

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1. Radovici, A., and Meller, O.: Encéphalo-myélographie liquidienne, Presse méd. **40**:1933, 1932.

2. Wustmann, O.: Experimentelle Untersuchungen über die Reliefdarstellung (Umrisszeichnung) des Zentralnervensystems im Röntgenbild durch Thoriumkontrastmittel, Deutsche Ztschr. f. Chir. **238**:529, 1933.

Moniz, Pinto and Almeida Lima,[3] Löhr and Jacobi,[4] Jessen and Licht[5] and Trias.[6] Similar results have been obtained in this clinic by S. T. Kwan of the department of surgery in conjunction with the department of radiology. Moniz with his co-workers and Löhr and Jacobi have reported the largest series of cases. These investigators stated that up to the time of reporting no patient had shown significantly unfavorable after-effects which could be attributed to the colloidal thorium dioxide.

The technical features of the procedure present some limitation to the use of colloidal thorium dioxide for visualizing cerebral arteries. The carotid artery should be exposed by surgical procedure prior to the injection. The colloidal thorium dioxide passes through the brain in from one to two seconds, so that the roentgenogram must be taken as soon as the injection is being completed. Injection into the carotid artery on one side gives satisfactory visualization of arteries of the homolateral cerebral hemisphere only. In that hemisphere the anterior and middle cerebral arteries are well filled, but the posterior cerebral artery is not filled.

The reports which have come to our attention deal only with patients in whom the cerebral circulation is presumably intact, and no bad effect was noted from the injection in those cases. The question was raised as to what would be the result of injecting colloidal thorium dioxide into the carotid arteries of patients with intracranial vascular lesions and whether in these cases the substance would enter the brain and cause damage. It is theoretically exceedingly unlikely that in such conditions colloidal thorium dioxide would ever reach the parenchyma of the brain, since the extravasation of blood elements from cerebral vessels seems to take place in a vascular area of stasis. The colloidal thorium dioxide could hardly be expected to penetrate this area of stasis but would be carried off at once in the actively flowing stream of blood into which it is injected.

The possibility of harm from intracarotid injections of colloidal thorium dioxide for arterial encephalography seems to lie in the more remote effects of thorium in the body. A year ago, the Council of Pharmacy and Chemistry of the American Medical Association[7]

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3. Egas Moniz; Pinto, A., and Almeida Lima: Le thorotrast dans l'encéphalographie artérielle, Rev. neurol. **32**:646, 1931.

4. Löhr, W., and Jacobi, W.: Die kombinierte Encephalo-Arteriographie, Arch. f. klin. Chir. **173**:399, 1932.

5. Jessen, H., and Licht, E. de F.: Ueber die arterielle Encephalographie, Acta psychiat. et neurol. **8**:209, 1933.

6. Trias, A.: Intracranial Arteriography in the Diagnosis of Brain Tumors, Rev. de cir. Barcelona **3**:36, 1932; abstr., Zentralbl. f. d. ges. Neurol. u. Psychiat. **65**:72, 1933.

7. Report of the Council on Pharmacy and Chemistry: Thorotrast, J. A. M. A. **99**:2183 (Dec. 24) 1932.

announced its decision against the intravenous use of colloidal thorium dioxide in the larger dosage needed for visualization of the spleen and liver (75 cc.). The reasons for that decision were the imperfect elimination of the substance from the body, its fairly high alpha ray activity, the possibility of further increase in radioactivity by partial conversion into mesothorium and radiothorium, and the possibility of sensitization of tissues to roentgen rays. The decision of the Council does not necessarily prohibit the use of colloidal thorium dioxide in the visualization of intracranial structures in view of the relatively small doses needed for this purpose. The same principle applies to other warnings against

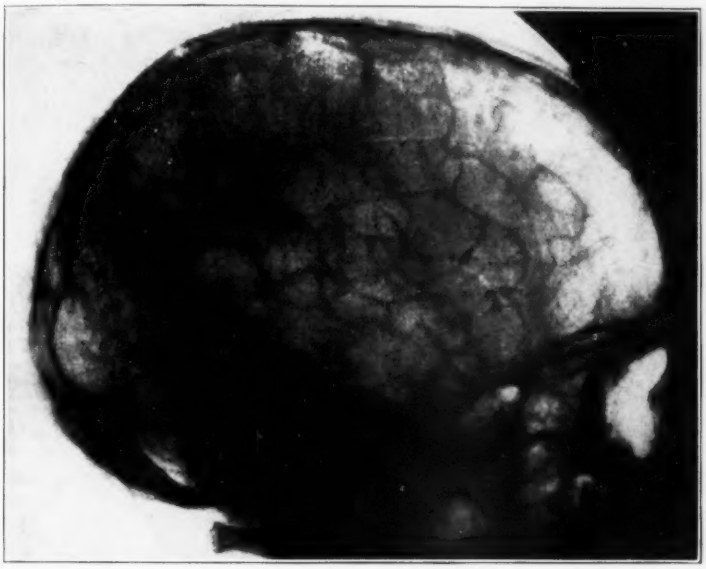

Fig. 1.—Normal cerebral arteries (reproduced by courtesy of Dr. S. T. Kwan).

the larger doses of colloidal thorium dioxide, for example, that it reduces the function of cellular immunity in the reticulo-endothelial system (Hanke [8]). A more serious possibility of harm was suggested by Shih and Jung,[9] who found that large doses of colloidal thorium dioxide lower the thrombocytic content of the blood in rabbits. It is conceivable that in cases of subarachnoid or cerebral hemorrhage intracranial bleeding

8. Hanke, H.: Experimentelle Untersuchungen biologischer Abwehrvorgänge bei Thoriumdioxydspeicherung des Reticuloendothels, Ztschr. f. d. ges. exper. Med. **85**:623 and 653, 1932.

9. Shih, H. E., and Jung, T. S.: Thrombocytopenic Purpura Hemorrhagica Produced Experimentally with Thorotrast, Proc. Soc. Exper. Biol. & Med. **29**:243, 1931.

might be prolonged by intracarotid injections. Again, this does not seem to be a valid contraindication, for the small dose of colloidal thorium dioxide has not yet been shown to have any appreciable effect on the volumetric determination of blood platelets. Furthermore, the mechanism of extravasation of blood from cerebral vessels—from the capillaries or from the smallest vessels in an area of stasis, according to Ricker [10] and Schwartz [11]—limits the possibility of platelets playing much of a part in its control. Finally, if a patient has a frank hemorrhage into the brain he usually dies, and in such a case the use of colloidal thorium dioxide would be futile, but it could not be held responsible for the fatal outcome.

Although it is theoretically unlikely that colloidal thorium dioxide would ever enter the brain in clinical diagnostic procedures, this question led to the injection of small amounts of the substance directly into the brains of dogs, in order to determine experimentally the way in which colloidal thorium dioxide is handled in the parenchyma of the brain.

EXPERIMENTAL INJECTION INTO THE BRAIN

From 0.1 to nearly 1 cc. of colloidal thorium dioxide (unbuffered preparation) under aseptic surgical conditions was injected into the left ectolateral or left suprasylvian gyrus of the brains of nine dogs anesthetized with ether. The dogs showed little or no general disability from the second day on. They were killed at varying intervals after the injection. Frozen sections of the brain stained by the Herxheimer, Spielmeyer, Cajal, Hortega and Bielschowsky methods were studied histologically. In some cases an examination was made of unstained preparations or of specimens stained only faintly with hematoxylin.

The wound of the needle puncture was visible on the surface of most of the brains. On section a hole of macroscopic dimensions was found at the site of injection in every brain; it contained some of the injected substance more or less mixed with coagulated blood and fibrin. The injection had been made in each case into the white substance, and in many of these brains the dorsal aspect of the hole produced by the injection followed in its outline the corticomyelin border of the gyrus.[12] In some cases the internal surface of the hole was smooth and even; in other cases it was irregular with necrotic walls. This difference did not appear to depend on the length of time elapsing after the injection, or on the slight differences in the amount of the substance injected. Another variable feature which seemed independent of these factors was a grayish discoloration of the white matter

10. Ricker, G.: Sklerose und Hypertonie der innervierten Arterien, Berlin, Julius Springer, 1927.

11. Schwartz, P.: Die Arten der Schlaganfälle des Gehirns und ihre Entstehung, Berlin, Julius Springer, 1930.

12. In human pathology, processes are known which are sharply limited at the corticomyelin border. In a case of Jakob's (Ztschr. f. d. ges. Neurol. u. Psychiat. **27**:290, 1915) an encephalitic process was sharply limited to the white substance, and in a case of Sittig's (Ztschr. f. d. ges. Neurol. u. Psychiat. **33**:301, 1916) a tuberculous process of the cortex was limited entirely to the gray matter. It may be that the corticomyelin border provides a physicochemical boundary.

in the neighborhood of the focus of injection. In some cases discoloration was not seen; in others it remained in the white substance of the same gyrus but spread chiefly in a sagittal direction, orally and caudally from the focus, and in another case it extended toward the base, spreading deep into the central white matter of the brain.

The results of the microscopic examination will be given for each dog separately.

Dog S.—This animal was killed one day after injection of 0.2 cc. of colloidal thorium dioxide. The focus had a sharp border which could be seen macroscopically. On microscopic examination the focus proved to be surrounded by a narrow rim of disintegrated tissue, and in its interstitial spaces were free granules of colloidal thorium dioxide. In this rim some phagocytes were already present and packed with granules of the injected substance. These phagocytes were rather scarce, and accumulations were found only toward the dorsal and ventral edges of the focus. Fixed glia cells had disappeared from this rim; the few remnants of their cell bodies showed a pronounced change (ameboidosis). Surrounding this rim on the outside was another narrow rim in which the specimen stained by the Cajal method showed an increase and enlargement of the large astrocytes and their syncytial connections; very few of these macroglia cells contained granules of colloidal thorium dioxide in their cytoplasm, and precisely these cells had lost their syncytial connections and showed different stages of ameboid dilapidation. In this second ring there were also granular cells of glial and of hematogenous origin, but these free granular cells did not form a continuous ring although they collected at some spots. Outside this ring was a wide area, spreading basally nearly down to the ventricle, in which there was a general increase of oligodendroglia as well as emigration of leukocytes, lymphocytes and polyblasts from the blood vessels. The myelin sheaths in this area were degenerated and decolorized. In the inner part of this area there were also collections of granular cells around some blood vessels. In this case there was incomplete impregnation with the Hortega stain.

Dog Q.—This animal was killed two days after the injection of 0.2 cc. of colloidal thorium dioxide. The focus was entirely surrounded by a continuous thick ring of granular cells, apparently largely of glial origin, densely packed with granules of the injected substance. No free granules of colloidal thorium dioxide were found in the tissue. Within this ring and immediately around it the macroglia cells were enlarged and increased in number. None of these fixed glia cells contained intracellular colloidal thorium dioxide. No ameboid cells were found. Further out in the focus the blood vessels showed lymphocytic infiltration (symptomatic inflammation), but only here and there were occasional leukocytes still present. Outside the granular ring many single granular cells were found, packed with granules of colloidal thorium dioxide, apparently on their way to the surrounding blood vessels. Some of the adventitial cells of these blood vessels already contained granules of colloidal thorium dioxide. At one place the injected substance was observed also in an endothelial cell. The myelin sheaths were degenerated and decolorized in a wide area around the focus, even in the white matter of the adjacent gyrus. The Hortega stain gave incomplete impregnation.

Dog R.—This animal was killed three days after the injection of 0.2 cc. of colloidal thorium dioxide. The masses of granular cells which surrounded the focus spread in great number ventrally through the central white matter of the brain toward the ventricle, but practically none of them passed dorsally toward

the surface of the brain, or stepped over the corticomyelin border. Thus the whole area from the white matter of the ectolateral gyrus, through the central white matter, to the dorsal surface of the lateral ventricle was densely filled with granular cells which were packed with granules of colloidal thorium dioxide. These granular cells collected around blood vessels, many of which were also infiltrated with lymphocytes. Granules of the injected substance were also found in adventitial cells, and many were seen in the endothelial cells of the blood vessels. The most remarkable feature was the collection of these granular cells also under the ependymal lining of the ventricle. Many granular cells were also found between the ependymal cells, breaking through the ependymal lining and thus even reaching the surface of the ventricular cavity. It seems probable that if lumbar puncture had been performed in this case granular cells filled with colloidal thorium dioxide would have been found in the spinal fluid. The myelin sheaths were degenerated in a wide area around the focus. In a somewhat smaller zone around the focus there was also destruction of the glial network. In that zone the specimens stained by the Cajal method revealed necrobiotic, ameboid cell bodies, while in somewhat more distant regions the macroglia was well preserved. The specimen stained by the Hortega method gave no satisfactory impregnation.

Dog L.—This animal was killed five days after the injection of nearly 1 cc. of colloidal thorium dioxide. In contrast to the preceding case, the surrounding reaction was limited to the immediate neighborhood of the focus. Encircling the focus was a rim of granular cells containing granules of colloidal thorium dioxide. These cells did not spread out into the environs but could be traced only to the nearest blood vessels, which showed only moderate lymphocytic infiltration and contained granules of colloidal thorium dioxide in some of their adventitial and endothelial cells. The macroglial network was not at all damaged. In the outer part of the rim and on its outer circumference the macroglia was increased, and many large and double nucleated macroglia cells, rich in processes, were found there. This well developed glial wall showed a little regressive change at only one place, namely, at the dorsal edge of the focus near the corticomyelin border, where a few ameboid cells were seen. However, these exceptions were but few in the otherwise complete ring of progressive macroglia. In accordance with these observations, the myelin sheaths were well preserved around the focus immediately outside the granulocellular rim.

Dog J.—This animal was killed six days after the injection of slightly less than 1 cc. of colloidal thorium dioxide. The examination disclosed changes similar to those seen in dog L, chiefly the absence of a widespread reaction around the focus. In two points there were slight differences: Granular cells around the focus contained granules of lipoid as well as of colloidal thorium dioxide, at times even in the same cells; a macroglial ring was not developed around the granulocellular rim, although the macroglial network was intact around the focus.

Dog O.—This animal was killed nine days after the injection of 0.2 cc. of colloidal thorium dioxide. In general the observations were the same as those on dog L. The increase of macroglia surrounding the rim of the focus was not continuous in this case. It was marked only at some places. On the other hand, the specimens stained by the Hortega method showed an increase of microglia at the outside of the granulocellular rim, in different stages of enlargement and in transformation into rounded forms. Evidently these microglia cells represented one of the sources of granular cells, among which they intermingled.

Dog P.—This animal was killed sixteen days after the injection of 0.1 cc. of colloidal thorium dioxide. The specimens showed the same changes as in dog L and also a slight increase of microglia near the focus.

Dog N.—This animal was killed thirty days after the injection of 0.1 cc. of colloidal thorium dioxide. In this case the focus was a small, collapsed hole, in the shape of a half-moon, which was situated at the corticomyelin border, and macroscopically appeared nearly empty. Seen microscopically the hole was bordered by a narrow rim of granular cells, containing colloidal thorium dioxide; these cells could be traced to the nearest blood vessels. The lymphocytic infiltration of these blood vessels was less marked than in the previous cases. Immediately outside the granulocellular rim the myelin sheaths and the axis-cylinders were entirely intact. The macroglial network was markedly increased outside the rim, but not equally so since it was more marked at the border next to the gray matter. Specimens stained by the Hortega method gave only incomplete impregnation.

Dog M.—This animal was killed sixty days after the injection of 0.5 cc. of colloidal thorium dioxide. After removal of the brain the focus still cast a shadow on the roentgen film. Seen macroscopically the focus appeared as a small, spindle-shape of a half-moon, which was situated at the corticomyelin border, and the left suprasylvian gyrus. Microscopic sections showed that the granulocellular rim was much narrower than in dog N and also that it had become discontinuous. At some places it was still made up of from five to twelve rows of cells. At some places, however, the rim was reduced to a single row or was even deficient; there the processes and cell bodies of the macroglial ring reached the surface of the hole. This shows that a large part of the substance had already been transported away. The granular cells filled with colloidal thorium dioxide were mixed with other granular cells containing lipoid; the latter were relatively increased in number. Both kinds of granular cells were found in the adventitia of the adjacent blood vessels. The increase of the macroglia cells and macroglial network in a zone outside the granulocellular rim had become still more marked. The most dense part of this network was at the cortical border of the focus. In the inner part of this zone the microglia was definitely proliferated, but this proliferation did not form an equally developed ring. The observation of greatest interest was the fact that axis-cylinders and myelin sheaths were entirely intact immediately outside the granulocellular rim. This indicated that these subtle structures were not damaged physicochemically by the colloidal thorium dioxide which was deposited in their immediate neighborhood for a period of two months.

COMMENT ON THE REACTION TO COLLOIDAL THORIUM DIOXIDE IN THE BRAIN

To serve as controls, two dogs received injections of iodized poppy-seed oil 40 per cent and four dogs, injections of olive oil [13] into the brain. The same general technic was observed. On histologic examination there proved to be no essential difference in the way in which the brain reacted

13. Tuthill and Beck (Reaction of Cerebral Tissue to Direct Injection of Oil, Arch. Neurol. & Psychiat. **29**:1263 [June] 1933) injected relatively large amounts of olive oil into the brains of rats and rabbits. Their results imply injection under such pressure as to make their observations not comparable with ours.

to these substances and to colloidal thorium dioxide, except that olive oil was taken up into the phagocytic cells more slowly than colloidal thorium dioxide or iodized poppy-seed oil 40 per cent.

The results of these examinations show that colloidal thorium dioxide acts as a foreign substance in the parenchyma of the brain, and no special chemical or physicochemical influence on the tissues could be demonstrated to come from colloidal thorium dioxide during the time of our observation with the methods at our disposal. The big difference in the reaction of the tissue which was found after injections of colloidal thorium dioxide alone lends further emphasis to this statement.

Two types of reaction stand out. One is a widespread diffusion of granular cells loaded with granules of colloidal thorium dioxide throughout an area in which the macroglial network is destroyed and the myelin sheaths and axis-cylinders show marked changes. The other is a sharply outlined focus separated from the surrounding normal tissue by a narrow wall of granular cells and sometimes encircled by a proliferation of slightly enlarged macroglia cells which form a dense network.

This difference in the type of reaction does not appear to depend on the amount of substance injected or on the length of time following the injection.[14] It is not a matter of a different stage or degree of tissue reaction, or of difference in transport of the injected material. The actual transport goes only to the blood vessels in the immediate neighborhood, never to the surface of the brain or to the ventricles. The explanation lies in purely mechanical factors. All the specimens with widespread diffuse reactions show definite signs of a mechanical explosive effect which is evident in all the tissues surrounding the focus. Thus, the manner of injection might be responsible for these differences in reaction. Also the respect for the corticomyelin border seems to contain a physicomechanical factor. In this way, too, the strange appearance of the brain of dog R is explained. Apparently the substance was driven by the injection through the whole central white matter of the brain to the ventricular surface, and there it even broke through the ependymal lining in some places. The granules of colloidal thorium dioxide were spread out over these places and taken up by the local and hematogenous phagocytes. Whether the granular cells which took up the colloidal thorium dioxide in the immediate neighborhood of and between the cells of the ependymal lining are mobilized ependymal cells or cells immigrating from the subependymal tissue cannot be decided in this case on account of the dense filling of the whole area between the site of injection and the ependyma by a continuous mass of granular cells.

14. Also in abscess of the brain, according to Knapp (Ztschr. f. d. ges. Neurol. u. Psychiat. **139**:49, 1932), the formation of the capsule is largely independent of the age of the abscess alone.

However the tissue reaction varied in certain respects as time went on, and some points are noted here which might serve as indicators of the age of the focus. The first phagocytic granular cells appear on the first day following the injection,[15] but they are still rather scarce and do not form a continuous ring around the injected substance; such a ring begins on the second day. Free granules of colloidal thorium dioxide are present in the tissue only on the first day and are absent from the second day on. Leukocytes appear on the first day following the injection; they disappear on the second day. The first appearance of the colloidal thorium dioxide in the adventitia and endothelium of the adjacent blood vessels is noted on the second day following the injection; from the third to the fifth day the transport to these blood vessels increases, and after this time it remains about stationary. This is interesting because in pathologic changes in man the transport of fat to the blood vessels in cases of fatty embolism does not begin until after six days, according to Müller,[16] who made the first systematic study on the timing of tissue reactions in the brain. In the dogs observed the first fatty products likewise appeared on the sixth day following the injection. The amount of colloidal thorium dioxide in the hole of the focus and in its granulocellular rim decreases markedly, beginning from the third week following the injection and continuing through the second month. Without doubt, the substance is being carried away from the brain by way of the blood vessels. Unfortunately, we did not examine the liver and spleen of the dogs. Still, after sixty days there was enough substance left in the granulocellular rim around the empty hole to cast a dense shadow on the roentgenogram. The proliferation of the fixed macroglial network is noticeable on the first day following the injection. This corresponds to Müller's observations in human vascular foci. This proliferation becomes still more marked from the fifth day on. Proliferation of mobile glial elements is noticeable from the first day on. Destruction, necrobiosis and ameboidosis of the macroglial elements are to be found only in a very acute stage within the first three days following the injection, not later. The same is true of the destruction of myelin sheaths and axis-cylinders which is found in some cases. This fits in with the hypothesis presented; namely, that these changes are caused by mechanical injury to the tissue.

15. This is in accord with an observation by Carmichael (J. Neurol. & Psychopath. **9**:209, 1929) that within a few hours after wounding (injection of the animal's own blood into its brain) products of degeneration begin to be removed by microglia cells. In human ischemic foci the first granular cells were observed forty-five hours after the infliction of damage by Müller.[16]

16. Müller, G.: Zur Frage der Altersbestimmung histologischer Veränderungen im menschlichen Gehirn unter Berücksichtigung der örtlichen Verteilung, Ztschr. f. d. ges. Neurol. u. Psychiat. **124**:1, 1930.

INJECTION INTO THE VENTRICLE

In order to determine the reaction of the ventricles, two dogs were given injections of colloidal thorium dioxide (unbuffered preparation) into the lateral ventricle.

Dog H.—This animal was killed one-half hour after the injection of 2 cc. of colloidal thorium dioxide into the left lateral ventricle. Free granules of colloidal thorium dioxide were closely adherent to the ventricular surface of the ependymal lining, but no granules had entered their cytoplasm. The contact was so close that the layer of granules followed every elevation made by the ependymal nuclei. This close adhesion is characteristic of the stage preceding phagocytosis, as Wen [17]

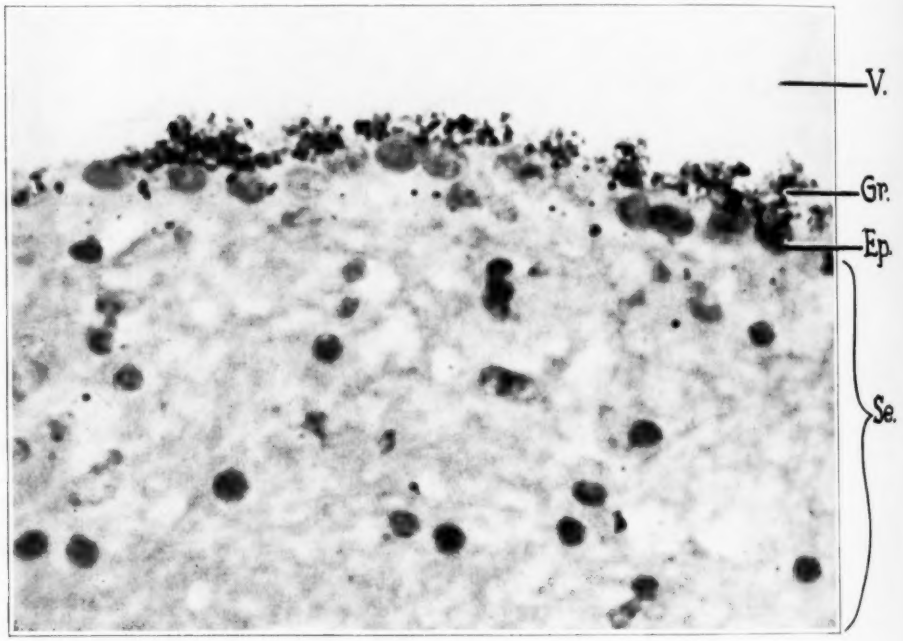

Fig. 2.—Specimen of brain of dog H, killed one-half hour after the injection of 2 cc. of colloidal thorium dioxide (unbuffered preparation) into the left lateral ventricle: *V.*, left lateral ventricle; *Gr.*, layer of granules of colloidal thorium dioxide closely adherent to the ependymal lining; *Ep.*, single layer of intact ependymal cells; *Se.*, subependymal layer.

pointed out for other cells. The ependymal cells showed no sign of reaction but formed only one continuous row. Some free granules of colloidal thorium dioxide were seen in some places between ependymal cells or in the subependymal tissue. None of these granules were taken up by cells. They were probably not carried there by the microtome knife during sectioning of the specimen.

Dog K.—This animal was killed ten days after the injection of 1 cc. of colloidal thorium dioxide into the left lateral ventricle. At necropsy, the ependyma showed

17. Wen, I. C.: Personal communication to the authors.

marked proliferation. In many places it was increased to five, ten or even fourteen rows of cells, most of them containing granules of colloidal thorium dioxide in their cytoplasm (fig. 3). These areas of proliferation and phagocytosis formed larger or smaller plaques. In addition to these plaques small villi were also found, resembling those of ependymitis granulosa. The small blood vessels in the subependymal layer showed a slight lymphocytic infiltration. This might bring up the question whether mesodermal or hematogenous elements could participate in the formation

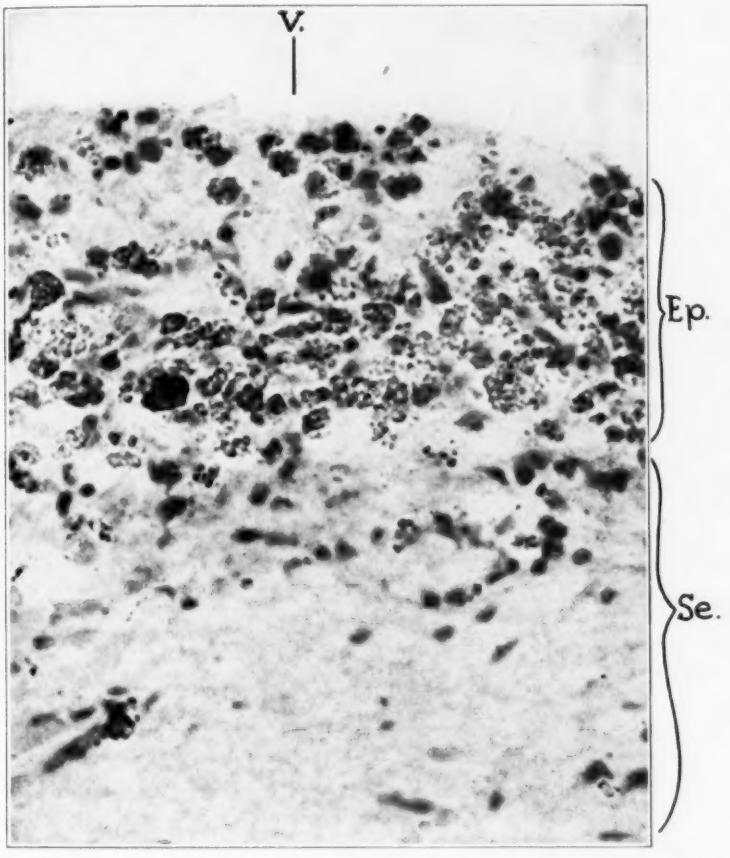

Fig. 3.—Specimen of brain of dog K, killed ten days following the injection of 1 cc. of colloidal thorium dioxide (unbuffered preparation) into the left lateral ventricle: *V.*, left lateral ventricle; *Ep.*, ependymal layer, thickened by proliferation of the ependymal cells to about ten rows of cells, in an area of an ependymal plaque; most of the cells in the ependymal layer are spherical and contain granules of colloidal thorium dioxide in their cytoplasm, thus being transformed into ependymogenous granular cells; *Se.*, subependymal layer.

of the ependymal plaques or villi. This question was long ago brought up for ependymitis granulosa, and the decision was against the mesodermal or hematogenous and in favor of the ependymal origin of these formations. Our observations also point to this conclusion: 1. The perivascular infiltration is so slight

that it could hardly be the source, or at least the only source, of the large number of granular cells found in these plaques. 2. No infiltration can be traced between many of these plaques and the nearest infiltrated blood vessel, and the only cells which can be followed in this space from the plaque to the blood vessel are granular cells already loaded with granules of colloidal thorium dioxide. It must be admitted that in many other places the continuity between the perivascular infiltrations and the plaques is more intimate, and it cannot be disproved that some of the granular cells may come from infiltrative cells. 3. The strongest argument is that cells which are surely ependymal and which are still connected with the ependyma show definite and unmistakable signs of proliferation as well as of phagocytosis. A good example is shown in figure 4. Cell *A* is unmistakably an ependymal cell

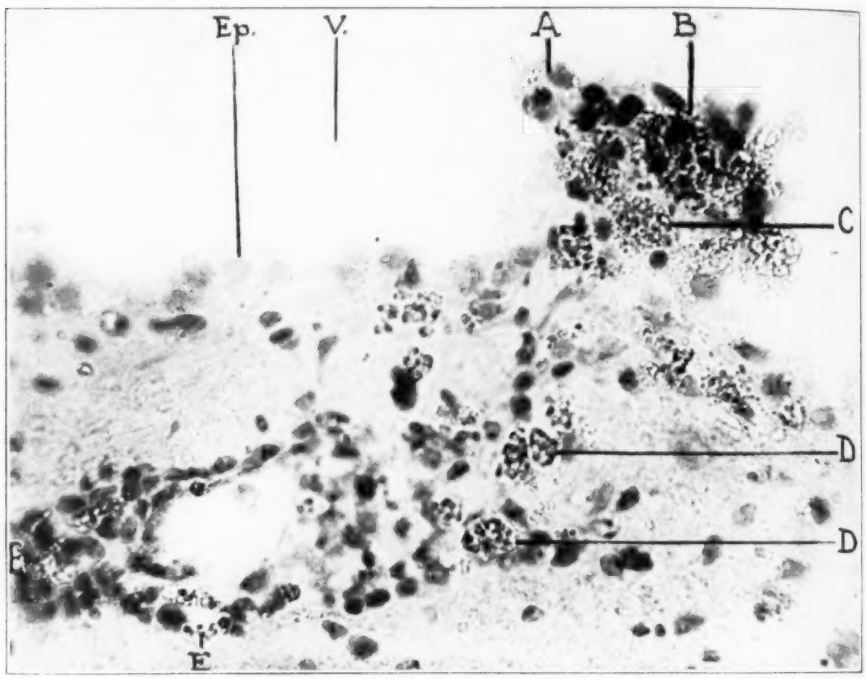

Fig. 4.—Specimen of brain of dog K, killed ten days after the injection of 1 cc. of colloidal thorium dioxide (unbuffered preparation) into the left lateral ventricle. Section through an ependymitic villus (in the right upper quarter of the figure): *V.*, left lateral ventricle; *Ep.*, single row of unaltered ependymal lining lateral to the ependymitic villus; *A*, an ependymal cell, still in continuity with the ependyma, at the top of the ependymitic villus, containing granules of colloidal thorium dioxide in its cytoplasm; *B*, granular cell in the second row of the ependymal lining, which still retains a connection with the ependyma at its upper part, but on the other side, directed toward the interior of the villus, is already becoming free; *C*, free ependymogenous granular cell, packed with colloidal thorium dioxide lying in the middle of the ependymal villus; *D*, granular cells half way from the villus to the blood vessel in the left lower quarter of the figure; *E*, adventitial cells of this blood vessel containing granules of colloidal thorium dioxide.

in contact with the ependyma at the top of an ependymal villus; it has granules of colloidal thorium dioxide in its cytoplasm. To the right of this cell and also in the surface row of the ependymal lining there are dark, longer, proliferating ependymal cells which are still in contact with the adjacent ependymal cells. In the second ependymal row there is a granular cell, *B*, which still retains a connection with the ependyma at its upper part, but on the other side, which is directed toward the interior of the villus, cell *B* is already becoming free. Cell *C* is a free granular cell packed with colloidal thorium dioxide lying in the middle of the ependymal villus. This cell undoubtedly has its origin in the ependyma. The cells marked *D* are granular cells half way from the villus to the blood vessel in the left lower quarter of the figure. The cells *E* are adventitial cells of this blood vessel containing granules of colloidal thorium dioxide.

Therefore it is evident that proliferation of the ependymal cells and their transformation into mobile, round, granular cells, which take up the granules of colloidal thorium dioxide from the ventricle, can take place and that these cells form at least an important part of the collections of granular cells found at the surface of the ventricle. It cannot be stated to what extent cells of other origin participate in the formation of these granular cells, if at all. Only their ependymal origin can be traced with certainty.

As a control, olive oil was injected into the ventricle of one dog.

Dog V.—This animal was killed seven days after the injection of about 0.2 cc. of sterilized olive oil into the left lateral ventricle. All the oil was still in the ventricular cavity. None of it was taken up by the ependymal cells, nor could any of it be found behind the ependymal lining or in the adventitial spaces. In many places the droplets of oil were closely adherent to the ependymal lining, but they were never found in the cytoplasm of the ependymal cells. The ependyma, however, showed heavy proliferative reactions with the formation of larger and smaller plaques and ependymal villi, many of which were covered with droplets of oil, but none of which contained the slightest trace of this substance within their cell bodies. At one place an interesting detail was found. At the top of a minute ependymal plaque of three rows of cells a droplet of oil lay covered on its ventricular side by a thin syncytium of flattened ependymal cells with four flat, longitudinally stretched, slightly curved nuclei. Thus the ependymal cells surrounded and included the droplet of oil as in a cystic cavity but did not take it into their cytoplasm. A small number of blood vessels of the subependymal layer showed slight lymphocytic infiltration.

COMMENT ON THE REACTION TO COLLOIDAL THORIUM DIOXIDE IN THE VENTRICLE

It is of interest to prove that granular cells can come from the ependyma, as is shown by our observations, because according to Walter [18] the question of the resorptive function of the ependyma is not yet decided. More recently, in a report before the Psychiatric Congress in Bonn, Spatz [19] went so far as to state that the ependyma has no

18. Walter, F. K.: Die Blut-Liquorschranke: Eine physiologische und klinische Studie, Leipzig, Georg Thieme, 1929.

19. Spatz: Vitale Färbung und Lehre vom Stoffaustausch zwischen Zentralnervensystem und übrigem Körper, Zentralbl. f. d. ges. Neurol. u. Psychiat. **64:** 241, 1932.

function as a barrier, because in Goldmann's [20] second experiment it was shown that dyes penetrate from the cerebrospinal fluid into the brain as into a structureless gel and that the penetration depends only on the dispersion of the dye solution. This conclusion stands in contradiction to some older statements in the literature. Following the injection of a 5 per cent solution of lithium carmine into the ventricles of young goats, Klestadt [21] found red-stained elements in the ependymal cells and also heavily laden "leukocytes," in part migrating through the epithelium and in part already located in the tissue of the brain. The same sort of ingestion by the ependyma and some migrating cells, which Klestadt considered to be leukocytes, were found after the injection of fat (sodium oleate, saturated in a 1 per cent saline solution). Glycogen was not taken up by the ependymal cells. Following the injection of india ink into the ventricles there was no phagocytosis of the particles of ink by the ependymal cells, but in some places the ependymal lining appeared interrupted by immigrating leukocytes packed with granules of ink. Thus, Klestadt first observed resorptive phagocytic functions of the ependyma. He also seems to have observed its proliferative changes, but he did not recognize them as such. His "packed leukocytes," or at least the larger part of them, are probably nothing else than mobilized ependymal cells becoming transformed into granular cells, which we have described in the foregoing statements.

Later, Wislocki and Putnam [22] carried out similar investigations in kittens after producing hydrocephalus experimentally. After the injection of potassium ferrocyanide and iron ammonium citrate into the dilated ventricles they found the lining of the ventricles stained macroscopically with prussian blue. On microscopic examination granules of prussian blue were found in the cytoplasm of the ependymal cells, in the intercellular, perineural and to a large extent in the perivascular spaces. Microscopically the trypan blue differed somewhat in distribution from the prussian blue; it was visible on the surface of the ependymal cells in some areas, but none was discernible in the cytoplasm of the ependymal cells. It was present, however, in adventitial cells surrounding the blood vessels of the brain. No reactive changes of the ependyma, such as proliferation or thickening, are mentioned.

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20. Goldmann, E. E.: Vitalfärbung am Zentralnervensystem, Beitrag zur Physio-Pathologie des Plexus chorioideus und der Hirnhaut, Berlin, G. Reimer, 1913.

21. Klestadt, B.: Experimentelle Untersuchungen über die resorptive Funktion des Epithels des Plexus chorioideus und des Ependyms der Seitenventrikel, Centralbl. f. allg. Path. u. path. Anat. **26**:161, 1915.

22. Wislocki, G. B., and Putnam, T. J.: Absorption from the Ventricles in Experimentally Produced Hydrocephalus, Am. J. Anat. **29**:313, 1921.

Nañagas [23] confirmed the statements of Wislocki and Putnam in regard to the intake of the granules of prussian blue from the ventricular surface, but he also did not find reactive changes of the ependyma; also his figures 3 and 4 (plate 51) show an unaltered, smooth ependymal lining of one row of cells.

Weed [24] confirmed the statements about granules of prussian blue, but following the injection of india ink he found the particles of carbon collected against the outer side of the cells of the ependyma, and yet there was no indication of any absorption.[25] Nevertheless the particles were also present in the perivascular spaces.

Stern [26] added no additional information about ependymal reactions to crystalloids or colloids.

The experiments described in this article give a further example of a substance which is taken into the ependymal cells, and they also provide evidence of the capacity of the ependyma to proliferate and produce mobilized phagocytic cells, for which we suggest the name "ependymogenous granular cells."

That the ependymal syncytium is able to proliferate is well known from the studies of Merle,[27] van Valkenburg [28] and others, especially French authors, in ependymitis and similar conditions. However, the ability of the ependyma to form free, mobilized granular cells has hitherto not been demonstrated.

This capacity is not brought out from the ependyma by all substances. Trypan blue (Wislocki and Putnam) and glycogen (Klestadt) are not taken into the ependyma and cause no reaction in it. Prussian blue (Wislocki and Putnam, Nañagas, Weed) brings out only phagocytosis by the ependymal lining with no proliferation. According to our observations, olive oil produces only ependymal proliferation without phagocytosis and without formation of granular cells. Colloidal thorium dioxide (unbuffered preparation) has a strongly stimulating influence on the ependyma, causing proliferation, phagocytosis and mobilization; apparently similar reactions are evoked by lithium carmine,

23. Nañagas, J. C.: Experimental Studies on Hydrocephalus, Bull. Johns Hopkins Hosp. **32**:381, 1921.

24. Weed, L. H.: The Absorption of Cerebrospinal Fluid into the Venous System, Am. J. Anat. **31**:191, 1923.

25. This statement is, however, in contradiction to the previous results of Klestadt.

26. Stern, L.: Les dernières recherches concernant le fonctionnement de la barrière hémato-encéphalique, Schweiz. med. Wchnschr. **59**:935, 1929.

27. Merle, P.: Etude sur les épendymites cérébrales, Thèse de Paris, no. 305, 1910; quoted by van Valkenburg,[28] p. 134.

28. van Valkenburg, C. T.: Experimentelles und Pathologisches über Ependym und Plexus chorioideus, Monatschr. f. Psychiat. u. Neurol. **73**:133, 1929.

sodium oleate and india ink, according to Klestadt's observations—if one applies our interpretation to his results. But according to the observations of Weed, india ink does not belong to this group.

The explanation of these differences is a matter of conjecture. Wustmann [2] discussed particularly the presence of a protective colloid rich in dextrin and the thorium dioxide in colloidal thorium dioxide. He also demonstrated the significant development of acidity in cerebrospinal fluid mixed with unbuffered colloidal thorium dioxide, which does not occur in mixtures with the buffered preparation. The application of this chemical information to the understanding of the ependymal reaction to colloidal thorium dioxide which is described in this report requires further study.

SUMMARY

On injection into the carotid artery, colloidal thorium dioxide allows visualization of cerebral arteries. It has been shown here by S. T. Kwan of the department of surgery in conjunction with the department of radiology that the procedure described by Moniz and modified by Löhr and Jacobi is feasible.

From the literature suboccipital or lumbar injection of colloidal thorium dioxide appears to have important possibilities in encephalography, but it has not been carried out here.

The ultimate effect of colloidal thorium dioxide on the body has not yet been determined.

Injection of colloidal thorium dioxide into the brains of dogs shows that it acts there as a foreign substance. No definite evidence of a special physicochemical destructive action on axis-cylinders or on myelin sheaths could be demonstrated histologically in examinations covering a period of two months following the injection. The colloidal thorium dioxide is transported from the parenchyma of the brain to adjacent blood vessels at a rather quick rate and is thus carried away.

The following points are of special interest in the microscopic examination. 1. After injection into the brain: (*a*) The extension of the lesion produced in the brain is largely dependent on mechanical factors attending the injection. (*b*) Free granules of colloidal thorium dioxide are present in the brain only on the first day. The first granular cells which carry off the granules of colloidal thorium dioxide appear on the first day in the brain tissue; on the second day following the injection the substance appears in the adventitia and endothelium of the adjacent blood vessels. (*c*) Leukocytic emigration is present on the first day and disappears on the second. 2. Following injection into the ventricle the granules of colloidal thorium dioxide are taken off by proliferating ependymal cells which become rounded, free, mobile granular cells (ependymogenous granular cells).

EXPERIMENTAL POLIOMYELITIS

CYTOLOGIC STUDIES OF THE CEREBROSPINAL FLUID AND THE RESPIRATORY METABOLISM OF THE EXCISED SPINAL CORD AND BRAIN

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AND
S. BERNARD WORTIS, M.D.
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Cellular changes appearing at some stages of experimental acute anterior poliomyelitis have been recorded on several occasions.[1] However, the changes that develop throughout the experimental disease have not been recorded, nor has the nonspecific arachnoiditis that follows intracerebral inoculation been taken into account.[2] Therefore it seemed important to report the changes in the spinal fluid that occurred in over one hundred Macacus rhesus monkeys at the various stages of the disease and to correlate these changes with the clinical manifestations and various experimental types of the disease.

EXPERIMENTAL DATA

Technic.—The spinal fluid was obtained from the cisterna magna of animals anesthetized with ether. Only the findings of clear taps were considered. To the spinal fluid was added an equal amount of 10 per cent solution of glacial acetic acid colored well with methylene blue, and after the mixture had been agitated for five minutes the counts were made in duplicate, using a Zeiss hemocytometer. The differential counts on specimens containing from 200 to 500 cells were made under high dry magnification and stained with ripened polychrome methylene blue

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Read at the Sixtieth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 6, 1934.

From the Departments of Bacteriology and Neurology of the New York University and Bellevue Hospital Medical College.

1. (*a*) Flexner, S., and Lewis, P. A.: Experimental Epidemic Poliomyelitis in Monkeys, J. A. M. A. **54**:1140 (April 2) 1910; J. Exper. Med. **12**:227, 1910. (*b*) Flexner, S., and Clarke, P. F.: Experimental Poliomyelitis in Monkeys, ibid. **56**:585 (Feb. 25) 1911. (*c*) Flexner, S.: Science **78**:129, 1933. (*d*) Naustaedter, M., and Thro, W. C.: New York M. J. **94**:813, 1911. (*e*) Gay, F. P., and Lucas, W. P.: Anterior Poliomyelitis, Arch. Int. Med. **6**:330 (Sept.) 1910. (*f*) Lucas, W. P.: Diagnosis of Infantile Paralysis in Prodromal and Acute Stage as Found in Experimental Study of Monkeys, Boston M. & S. J. **163**:245, 1910. (*g*) Harmon, P. H.; Shaughnessy, H. J., and Gordon, F. B.: J. Prev. Med. **5**:115, 1931.

2. Widal, and Merklen: Bull. et mém. Soc. méd. d hôp. de Paris **16**:899, 1899. Nissl, Franz: Zur Histopathologie der paralytischen Rindenerkrankung, in Nissl, and Alzheimer: Histologische und histopathologische Arbeiten über die Grosshirnrinde, Berlin, Julius Springer, 1904, vol. 1, p. 315.

or hematoxylin and eosin after fixation with iodine according to the method of Cunningham and Kubie.[3]

Globulin was tested for by the Pandy or Noguchi methods. The temperatures of the monkeys were taken by rectum and recorded in degrees Fahrenheit.

Observations on Control Animals.—Examination of the spinal fluids of one hundred normal monkeys showed that eighty had no cells, while the other twenty had between 1 and 6 cells. The test for globulin was negative for all. Following this test, punctures were performed on three monkeys daily for from four to seven consecutive days; in no instance did pleocytosis develop. Punctures were performed on one of these animals later five times on consecutive days. The first three specimens showed no cells, while the last two specimens showed 10 cells per cubic millimeter, but no increase in globulin. It is apparent then that repeated puncture in itself does not produce significant changes in the spinal fluid.

Total and differential blood cell counts were attempted but not carried on because it was not possible to establish a normal base line for any one animal.

In order to determine the effect of intracerebral inoculation on the spinal fluid count, the fluids from eleven animals were examined up to eight days after

TABLE 1.—*Cell Count of Spinal Fluid Following Sterile Intracerebral Inoculation with Emulsion of the Spinal Cord*

Monkey	1 Day	2 Days	3 Days	4 Days	5 Days	6 Days	7 Days	8 Days
1	385	110	...	...	...	...	...	...
2	46	50	...	...	...	...	...	15
3	262	360	...	12	...	...	...	...
4	106	...	...	504	148	...	...	...
5	90	...	...	128	6	...	...	...
6	...	...	...	120	0	...	...	...
7	185	...	...	34	16	...	...	...
8	...	...	7	...	...	...	...	...
9	...	...	4	...	...	...	...	...
10	...	...	...	0	...	...	...	...
11	...	...	...	10	...	...	...	...

the simple mechanical process of inoculation with sterile emulsion of the spinal cord. The results are given in table 1.

It is evident that the arachnoiditis following intracerebral trauma lasts for at least five days and even up to the eighth day. An animal killed twenty-four hours after intracerebral inoculation with suspension of sterile cord showed a dense infiltration of the subarachnoid space.

Obviously nonspecific factors may influence the cell count within eight days after intracerebral inoculation. Therefore in the following examinations the animals were used which (1) had periods of incubation of more than eight days or (2) had been infected by other routes, such as intranasally, or through the sciatic nerve or skin.

Observations on the Spinal Fluid in Different Stages of Experimental Poliomyelitis.—The cerebrospinal fluid counts were made at various stages of the disease. Table 2 shows the minimum and maximum counts and the average at each stage.

The cerebrospinal fluid count usually showed a progressive increase, most often reaching its maximum at the stage of extensive or complete paralysis. In the

3. Cunningham, R. S., and Kubie, L. S.: Fixation of the Cells of the Cerebrospinal Fluid with Iodine Vapor, Arch. Neurol. & Psychiat. **15**:761 (June) 1926.

preparalytic stage the count was lower when a rise of temperature was the only manifestation of the disease. Occasionally the maximum cell count was obtained in the late preparalytic or in the very early paralytic stage.

Relationship Between Cell Count and the Severity of the Disease: The average cell count at the different stages of the disease in thirty-nine animals in which complete and rapid paralysis had developed were compared with the counts on

TABLE 2.—*Cerebrospinal Fluid Cell Counts at Each Stage of the Experimentally Produced Disease*

Stage of the Disease	Minimum Count	Maximum Count	Average Count
Preparalytic stage	0	850	190
Paralysis	0	810	278
Height of paralysis	15	1,400	270

TABLE 3.—*Relation Between the Severity of the Disease and the Spinal Fluid Cell Count*

		Preparalytic Stage			Stage of Progressive Paralysis			Height of Disease		
Animal	Degree of Paralysis	Minimum Count	Maximum Count	Average Count	Minimum Count	Maximum Count	Average Count	Minimum Count	Maximum Count	Average Count
39	Complete and rapid paralysis	13	850	245	14	810	415	50	1,400	415
6	Slowly progressive paralysis	..	...	...	0	100	58			
14	Partial paralysis	0	675	135	..	...	...	0	300	93
28	No paralysis	..	...	...	..	...	...	14	160	61

TABLE 4.—*Differential Cellular Content of Spinal Fluid in Different Stages of Experimental Poliomyelitis*

	Percentage of Polymorphonuclears			Percentage of Mononuclears			Percentage of Bilobed Cells		
Stage of Disease	Minimum Count	Maximum Count	Average Count	Minimum Count	Maximum Count	Average Count	Minimum Count	Maximum Count	Average Count
Preparalytic; rise of temperature only	5	75	26.2	35	95	72.6	0	5.5	1.2
Preparalytic with symptoms	0	60	27	39.4	100	71.6	0	5	1.4
Progressive paralysis	2	65	29	39.4	98	70	0	4.3	1.0
Height of the disease	3	88	30.6	12	96.5	69	0	2.5	0.4

fourteen animals which showed partial paralysis, on six in which a slowly progressive paralysis extending over several days or longer developed and on eight which exhibited no paralysis (table 3).

Differential Count at the Various Stages of the Disease: In table 4 are given the differential counts at various stages of the disease. The type of cell is described under three headings: polymorphonuclear leukocytes, mononuclears (including all the cells having a nonsegmented nucleus, such as lymphocytes, monocytes, plasma cells, endothelial and giant cells) and bilobed cells (cells with a segmented or double nucleus). Both the average and extreme counts are given.

There are obviously wide fluctuations in the percentage of the various types of cell at any stage of the disease, and the average for each stage is approximately the same. There is no distinguishing differential cellular picture at any stage of the disease.

When mononuclear cells predominated in the preparalytic stage this predominance was maintained throughout the disease in any given animal. Occasionally there was a change to the polymorphonuclear type of cell; for example, one animal in the preparalytic stage had 360 cells, practically all of which were lymphocytes, but with the onset of paralysis 59 per cent of the 360 cells had become polymorphonuclear.

When polymorphonuclear cells were in the majority in the preparalytic stage they usually changed to the mononuclear type with the onset of paralysis. Occasionally the former type predominated in all the stages of the disease.

Changes in the Spinal Fluid Subsequent to Paralysis: The spinal fluids of three completely paralyzed and of twelve nonparalyzed animals were followed from the height of the disease until the spinal fluid count became normal. In the mild or nonparalytic condition the cell count became normal between the third and tenth days after the height of the disease, the average time being seven days. In the severely paralyzed animals the cell count did not reach the normal level until the fourth week after the onset of the paralysis.

In approximately half the monkeys an increased amount of globulin persisted for a longer time than did the increased cell count.

Spinal Fluid Count in Relation to the Clinical Syndrome: Other investigators[4] have reported a rise of temperature in the early stages of the experimental disease. In our series of sixty-four monkeys, seven showed a rise of temperature three days before the onset of symptoms; nineteen showed such a rise two days, twenty animals from one to one and a half days, and four animals twelve hours, prior to the onset of symptoms. In eight animals the symptoms and rise of temperature occurred at the same time, while in six the first indication of the disease was paralysis.

With the onset of paralysis the temperature often began to drop, becoming normal or even subnormal at the stage of complete paralysis.

Often the temperature showed a considerable rise (from 105 to 106 F.) for from twenty-four to forty-eight hours, with or without symptoms, reached a normal level and rose again with the onset of symptoms.

To determine whether a rise of temperature or pleocytosis is the first manifestation of the disease puncture was performed during the preparalytic stage on sixteen animals which showed a high temperature but no symptoms. The spinal fluids of only two of the monkeys showed an increased cell count, and in neither of the two was there an increased amount of globulin. Of the remaining fourteen animals, ten showed no increased cell count and the others showed 2, 3, 5 and 6 cells, respectively. During the next twenty-four hours pleocytosis developed in ten of the fourteen animals.

The course of the experimental disease, therefore, is as follows: Following a period of incubation of from three to seven days, the temperature rises from 2 to 6 F. From twelve to thirty-six hours later, pleocytosis develops, and symptoms appear either immediately or up to forty-eight hours later. These symptoms, which are indicative of involvement of the central nervous system consist of any one or a

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4. Kramer, S. D.; Hendrie, K. H., and Aycock, W. L.: J. Exper. Med. **51**: 933, 1930. Lucas.[1f] Harmon, Shaughnessy, and Gordon.[1g]

combination of the following: a change in facial expression, puckering of the mouth, irritability or apathy, ruffling of the hair, inertia and slowness, jumpiness and excitement, and later tremors of the head and ataxia. In no instance was any stiffness of the neck or back present. Paralysis may set in almost immediately or be delayed up to thirty-six hours after the onset of the symptoms. Usually prostration occurred from twelve to twenty-four hours after the onset of paralysis.

Occasionally the pleocytosis may appear much later in the paralytic stage. In several instances it did not develop until paralysis had already set in, and in one monkey it was not evident until the late paralytic stage. Another animal showed definite paralysis and typical histopathologic changes in the spinal cord but no cellular changes developed in the spinal fluid. An increased globulin content usually developed later than the increase in cells; two animals in the paralytic stage had positive tests for globulin in the absence of cells.

TYPES OF EXPERIMENTAL POLIOMYELITIS

The types of disease encountered in over three hundred and fifty monkeys with poliomyelitis were as follows:

1. *Nonparalytic Types.*—In twenty-four animals which received a "subinfective" dose of virus or partially neutralized mixtures of virus and serum paralysis failed to develop but definite evidence of poliomyelitis appeared. Three definite types were encountered: (*a*) Cases showing only changes in the cerebrospinal fluid. There were three such experimental cases and the cell count ranged from 14 to 160.

(*b*) Those showing changes in the cerebrospinal fluid and increase in temperature. There were ten such cases and the spinal fluid cell count ranged from 14 to 102.

(*c*) Those showing changes in the cerebrospinal fluid, increase in temperature and symptoms. About eleven cases come into this category. The animals showed a definite rise of temperature of from 2 to 4 F.; this was followed by pleocytosis ranging from 22 to 125 and then by symptoms analogous to those of the preparalytic stage, i. e., a change of expression and voice, irritability or drowsiness, ruffling of the hair, inertia, slowness of locomotion and often jerky incoordinate movements or a limp. In many cases the increase of temperature was as great as in the severe form of the disease.

As in the paralytic cases, the differential cerebrospinal fluid picture showed considerable variation, with extremes of from 5 to 65 per cent polymorphonuclear cells. Therefore, as already pointed out, the only indication that paralysis would not develop was the lower cell count during the course of the disease.

2. *Paralytic Types.*—(*a*) A severe and rapid course, with a preparalytic stage. This is the usual experimental form and has already been described. The typical course is summarized in chart 1.

(*b*) Progressive slow paralysis. Paralysis may ascend or descend and extends over the course of a week; in one instance it progressed for eleven days.

(*c*) Partial paralysis of one or more limbs.

(*d*) The diphasic type. Following a definite rise of temperature, with or without symptoms, the temperature dropped to normal usually for from twenty-four to forty-eight hours. However, in one instance it remained normal for eight days. Following this period of normal temperature there was a second rise with the development of symptoms and paralysis. The cerebrospinal fluid usually showed changes after the initial febrile response. A typical example is shown in chart 2.

(*e*) Bulbar and bulbospinal forms. Forms were encountered in which paralysis of the fifth, seventh and tenth cranial nerves was present in addition to paralysis of the limbs. There was only one strictly bulbar case. The animal had paralysis of the vocal cords and recovered. The facial nerve is the most commonly affected cranial nerve in these animals.

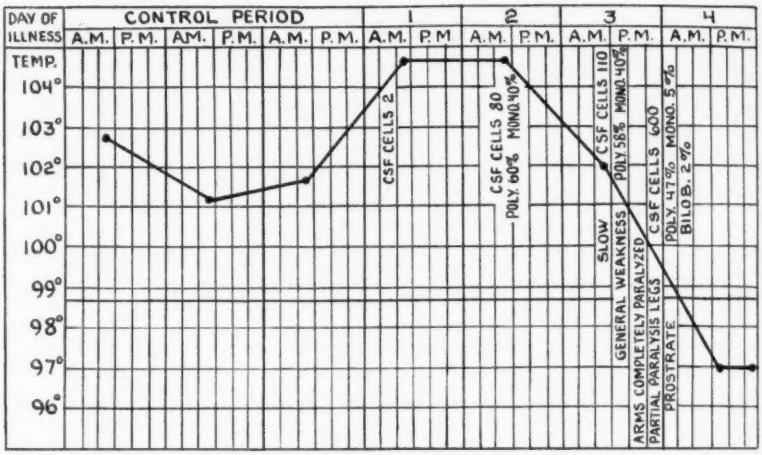

Chart 1.—Chart for temperature in the rapid paralytic type of experimental poliomyelitis.

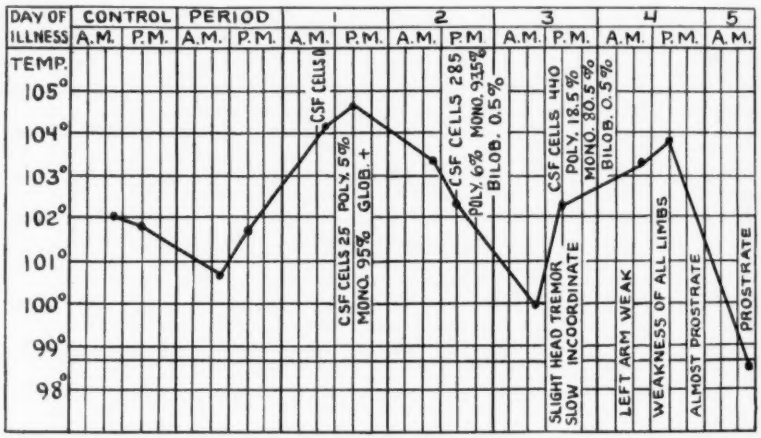

Chart 2.—Chart for temperature in the diphasic type of experimental poliomyelitis.

(*f*) Encephalomyelitic cases. A single case of involvement of the brain as well as of the cord was encountered. This has been recorded elsewhere.[5] It is important to note that no cases of encephalitis were encountered, although in the majority of cases the virus was inoculated directly intracerebrally.

5. Brodie, M.: Cerebral Involvement in Acute Anterior Poliomyelitis, Am. J. Dis. Child. **48**:57 (July) 1934.

(*g*) Cases with recrudescence of symptoms. Two such cases were observed. In one the monkey had a nonparalytic attack with pleocytosis (120 cells), increase of temperature and symptoms. This attack persisted for only two or three days, and the symptoms and changes in the spinal fluid subsided, only to be followed by a second attack, ten days after the first, with complete and rapid paralysis. In the second case, the animal was recovering from the initial paralysis when, ten days later, a recurrence of symptoms and extension of the paralysis occurred.

COMMENT

This experimental study, we believe, helps to explain some of the differences in the clinical reports of poliomyelitis in man. Some observers [6] have reported a predominance of lymphocytes in all the stages of the disease; others found this to be the case in the early stages of the disease, whereas in the paralytic stage the majority of the cells are said to be of the polymorphonuclear type. Still others reported to the contrary (i. e., polymorphonuclears early in the disease; later, lymphocytes [7]). Some [8] reports indicate that there is no typical differential picture.

In these experimental studies it was observed that for a period of almost a year the fluids obtained in the early stages showed a predominance of polymorphonuclear cells and that with the onset of the paralysis lymphocytes were in excess. Then followed a period (the same strain of virus was used and was equally potent) during which all the fluids examined contained mainly mononuclear cells. It is obvious, then, that

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6. (*a*) Lucas, W. P.: The Non-Specificity of the Cyto-Findings in the Spinal Fluid in Various Conditions, Especially in Children, Am. J. Dis. Child. **1**:230 (March) 1911. (*b*) Zingher, A.: The Diagnosis and Serum Treatment of Anterior Poliomyelitis, J. A. M. A. **68**:817 (March 17) 1917. (*c*) Meals, R. W., and Bowen, A. G.: J. Lab. & Clin. Med. **13**:411, 1932. (*d*) Sophian, A.: Arch. Pediat. **28**:201, 1911.

7. (*a*) Rührah, J.: Am. J. M. Sc. **153**:178, 1917. (*b*) Durham, H. G.: After-Care of Infantile Paralysis Cases of the 1916 Epidemic in Brooklyn, J. A. M. A. **80**:224 (Jan. 27) 1923. (*c*) Lyon, G. M.: Cytolysis in the Cerebrospinal Fluid in Acute Poliomyelitis, Am. J. Dis. Child. **40**:36 (July) 1928. (*d*) Résumé of Report of Poliomyelitis in Manitoba 1928, Canad. Pub. Health J. **20**:225 (May) 1929. (*e*) Campbell, G. A., and Mirsky, S.: ibid. **21**:375 (Aug.) 1930. (*f*) McNamara, J., and Morgan, F. G.: Lancet **1**:469 (Feb. 27) 1932.

8. (*a*) Draper, G., and Peabody, F. W.: A Study of the Cerebrospinal Fluid and Blood in Acute Poliomyelitis, Am. J. Dis. Child. **3**:153 (March) 1912. (*b*) Fraser, F. R.: J. Exper. Med. **18**:242, 1913. (*c*) DuBois, P. L.: Arch. Pediat. **33**:856, 1916. (*d*) Neal, J. B.; Abramson, H. L., and Associates: A Study of Poliomyelitis, Arch. Int. Med. **20**:341 (Sept.) 1917. (*e*) Dickie, W. M.: The After-Care of Poliomyelitis, J. A. M. A. **91**:1417 (Nov. 10) 1925. (*f*) Thelander, H. E.; Shaw, E. B., and Limper, M.: The Spinal Fluid Cytology in Poliomyelitis, Am. J. Dis. Child. **42**:1117 (Nov.) 1931. (*g*) Gosling, R., in Poliomyelitis, Report by International Committee for the Study of Infantile Paralysis, Baltimore, Williams & Wilkins Company, 1932.

for conclusive data a sufficiently large series of fluids must be examined over a long period of time.

Although some authors [8b] have maintained that in the human disease there is no correlation between the pleocytosis and the severity of the disease, others [9] have reported that such a relationship exists. In some epidemics there are many bulbar cases; in these the spinal fluids usually show a low cell count and the mortality is high; other epidemics include many cases of meningeal type with a high cell count but a low mortality.[10] Experimental bulbar types are rare, and experimental meningeal forms are never encountered. It is possible that in cases of the spinal type there is a correlation between the cerebrospinal fluid cell count and the degree of paralysis. There is further experimental evidence to substantiate this, for the spinal cords of animals with a low cell count showed considerably less destruction of nerve cells and cellular infiltration than those of animals with higher counts.

In the human disease, as in the experimental, the cell count may be normal.[11] Some workers have found (as in the experimental cases here reported) that although a normal cell count may be present early in the disease, a subsequent puncture may show pleocytosis.[12] Therefore the necessity of repeating the examination of the spinal fluid in the nonparalytic stage is apparent.

In the experimental disease a rise of temperature is the first manifestation of infection. In both human and experimental poliomyelitis, preparalytic signs and symptoms and even paralysis may be present in the absence of pleocytosis.[13] It is evident, therefore, that the pathologic process begins in the cord rather than in the meninges.[14] This is further confirmed by the fact that one animal showed no pleocytosis during the course of the disease, although histologic examination of the cord at the height of the disease showed the usual changes in the gray matter. The subarachnoid space was free from cells.

Further observations in this direction are as follows: 1. The cells in the subarachnoid space are usually deposited about the blood vessels and are of the same type as those in the perivascular spaces of the cord. Thus it appears that the source of the cells in the meninges is from the

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9. McDonald, S. F.: M. J. Australia **1**:1 (Jan. 7) 1933. Footnote 7*d*.

10. Neal, J.: Personal communication to the authors.

11. (*a*) Collier, J.: Lancet **1**:321, 1927. (*b*) Collis, W. A. F.: ibid. **1**:927, 1927. (*c*) Clarke, F., and Dow, A. G.: Rosenow's Serum in Prevention of Paralysis in Anterior Poliomyelitis, J. A. M. A. **83**:42 (Aug. 9) 1924. (*d*) Levinson, S. D.: J. Pediat. **3**:337, 1932. (*e*) Trask, J. D., and Harper, P. A.: Yale J. Biol. & Med. **5**:155, 1932. Meals and Bowen.[6c] Neal.[8d] McDonald.[9]

12. McDonald.[9] Levinson.[11d] Trask.[11e]

13. Meals.[6c] Levinson.[11d] Trask.[11e]

14. Schröder, P.: Deutsche med. Wchnschr. **51**:973, 1925. Hurst, E. W.: J. Path. & Bact. **32**:457, 1929.

perivascular spaces of blood vessels rather than an inflammation of the pia-arachnoid.

2. In confirmation of the results of other workers, monkeys could not be infected by the injection of large quantities of cerebrospinal fluid taken from patients in the preparalytic stage of the disease.

3. It is known that an inflammatory process in the meninges results in an increase of protein. The cerebrospinal fluid of only two of nine children with preparalytic and early paralytic stages showed an increase in total protein. Occasionally experimental animals with a considerable pleocytosis showed no increased globulin.

All this fits in with previous experiments,[15] indicating that in the experimental disease the passage of the virus is by way of the nerve fibers of the central nervous system rather than by way of the subarachnoid space.

The different types of the disease encountered in the experimental animal coincided closely with those in man. The nonparalytic (often erroneously called "abortive") type constitutes a high proportion of the human cases. The accepted criteria for such cases are: (1) a rise of temperature; (2) signs and symptoms in the central nervous system; (3) pleocytosis. Such types of the disease were found experimentally. However, in epidemics of poliomyelitis, mild "abortive" cases with disturbances in the upper respiratory or gastro-intestinal tract without clinical evidence of any involvement of the central nervous system are encountered. Poliomyelitis virus has been isolated from the throats of such patients [16] and later antibodies [17] had been demonstrated in the blood. Experimentally, several animals showed indefinite symptoms and a rise in temperature without pleocytosis. However, there was no way of proving that these cases were mild infection or "abortive" poliomyelitis, for immunity does not always develop in definitely nonparalytic cases. Moreover, even frank paralytic cases in man and experimental animals may fail to show a pleocytosis. Therefore, failure to find changes in the spinal fluid does not rule out the possibility of poliomyelitis infection.

In view of such observations and in keeping with the conception of poliomyelitis as a disease entirely affecting the central nervous system,[15] such cases are probably mild infections of the cerebrospinal axis rather than slight general invasion with the virus of poliomyelitis, as Paul and Trask [18] have supposed. These authors concluded that the "abortive" types were analogous to the first stage of general infection of

15. Brodie, M., and Elvidge, A. R.: Science **79**:235, 1934.

16. (*a*) Taylor, E., and Amoss, H. L.: J. Exper. Med. **26**:745, 1917. (*b*) Paul, J. R.; Salinger, R., and Trask, J. D.: "Abortive" Poliomyelitis, J. A. M. A. **98**:2262 (June 25) 1932.

17. Trask, J. D., and Paul, J. R.: J. Exper. Med. **58**:531, 1933.

18. Trask and Paul.[17] Paul, Salinger and Trask.[16b]

the diphasic type of poliomyelitis. We have found, however, that when the virus fails to reach the central nervous system after intranasal inoculation of animals with cut olfactory nerves, immunity to poliomyelitis rather than paralysis develops.

Of the paralytic forms the rapid spinal type with a prodromal period requires no further comment. However, a number of experimental animals had no preparalytic syndrome, and the first indication of the disease was paralysis. Such cases are encountered in the human disease.[19] Some observers have computed the value of serum therapy by comparing the incidence of paralysis in patients treated with serum with those untreated, thus comparing a less severe with a more severe group of cases. This was borne out in the epidemic in New York in 1931,[20] in which the mortality in cases observed in the nonparalytic stage, with or without treatment, was 2 per cent, while the total mortality in all cases of poliomyelitis in this epidemic was approximately 12 per cent. Therefore, many cases showing paralysis probably presented no prodromal symptoms, and many such cases would be classed in the so-called control group.

Another form of experimental poliomyelitis worth mentioning was a slowly progressive type, very much like Landry's ascending paralysis. One animal showed progressive paralysis for five days, but histologic examination revealed nothing unusual and no indication of active poliomyelitic cellular changes, comparable with the negative observations described in many cases of Landry's ascending paralysis in man.[21] However, animal passage of the cord proved that the condition was poliomyelitis. This, to our knowledge, is the first case of acute ascending paralysis proved to be due to the virus of poliomyelitis.

The experimental diphasic types are similar to those which occur in man, first described by Medin[22] and Wickman,[23] and are often

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19. Romer, P. H.: Epidemic Infantile Paralysis, New York, William Wood & Company, 1913. Tebbutt, A. H., and Helms, K.: A Report of the Epidemic of Poliomyelitis in New South Wales, 1931-1932, M. J. Australia **1**:43 (Jan. 14) 1930. Jenkins, R. B.: Canad. Pub. Health J. **20**:219, 1929. Wilson, May G.: Prodromal Symptoms of Infantile Paralysis, Am. J. Dis. Child. **13**:506 (June) 1917.

20. Park, W. H.: Therapeutic Use of Antipoliomyelitis Serum in Preparalytic Cases of Poliomyelitis, J. A. M. A. **99**:1050 (Sept. 24) 1932.

21. Wortis, S. B.: Landry's Paralysis and Acute Ascending Myelitis, in Nelson Loose-Leaf Living Medicine, New York, Nelson & Sons, 1931, vol. 6. Wortis, S. B., and Brock, S.: Cranial Neuritis, New York State J. Med. **34**:88, 1934.

22. Medin, O.: Ueber eine Epidemie von spinaler Kinderlähmung, Verhandl. d. internat. med. Kong. 1890, vol. 2, pt. 6, p. 37.

23. Wickman, I.: Acute Poliomyelitis, Nervous and Mental Disease monograph 16, New York, J. Nervous and Mental Disease Publishing Company, 1913.

incorrectly termed "dromedary" types.[24] As Draper [24] and Campbell and Mirsky [7e] have pointed out for man, so likewise in the experimental type the spinal fluid is normal during the first stage of the disease. Since these types occur experimentally when the disease is entirely neurotropic, there can be no reason for assuming a general systemic invasion in the human form of the disease; the first manifestations are probably due to the implantation of the virus in the central nervous system.

OBSERVATIONS ON THE RESPIRATORY METABOLISM OF TISSUE EXCISED FROM THE BRAIN AND SPINAL CORD

The respiratory metabolism was measured in the excised brain and spinal cord of normal monkeys and of animals experimentally infected with poliomyelitis. The Barcroft-Warburg manometric technic was used.

The cortex of the brain and the spinal cord were removed while the animal continued to breathe; the meninges and blood vessels were then stripped from the tissue and the tissue was minced. Small amounts (approximately from 100 to 150 mg.) of the tissue were then placed in the Warburg manometric vessels and immersed in Ringer's phosphate solution, with and without addition of dextrose, in physiologic concentration. The solutions were then buffered to p_H 7.4 and all the experiments were carried out at 37.5 C.

By this technic both the respiratory quotient and the intake of oxygen by the tissue were measured over a two hour period. In addition, chemical analyses of the brain, spinal cord, blood and spinal fluid were made for the quantitative determination of sugar and lactic acid content. For lactic acid the method of Friedemann, Cotonio and Shaffer was used; and for sugar, that of Hagedorn and Jensen.

Previous reports by Holmes, Dickens, Himwich,[25] Wortis [26] and others have shown that the respiratory quotient of normal brain tissue is 1.0, indicating utilization of either dextrose or lactic acid. This was confirmed for normal tissue of the cortex of the brain in Macacus rhesus.

The respiratory quotient is a measure of the nature of the foodstuff being burned by any living tissue. For carbohydrate or lactic acid oxidation, the respiratory quotient is 1.0; for protein, 0.80; for fat, 0.70.

Each animal tissue under normal conditions has its specific respiratory quotient. By the Barcroft-Warburg technic the respiratory quotients of other animal tissues have been measured. For example, in plain Ringer's phosphate solution, p_H 7.4, the respiratory quotient of human or rat brain is 1.0; of kidney, 0.85; of testis, 0.72; of liver, 0.77.

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24. Draper, G.: Acute Poliomyelitis, Philadelphia, P. Blakiston's Son & Co., 1917.

25. Himwich, H., and Goldfarb, W.: Proc. Soc. Exper. Biol. & Med. **30**:903, 1933.

26. Wortis, S. B.: Am. J. Psychiat. **13**:725 (Jan.) 1934.

TABLE 5.—*Respiratory Metabolism of Tissue from the Brain and from the Spinal Cord*

Subjects	Experiment	Respiratory Quotients: Brain: Plain Ringer Phosphate	Respiratory Quotients: Brain: Dextrose Ringer Phosphate	Respiratory Quotients: Spinal Cord: Plain Ringer Phosphate	Respiratory Quotients: Spinal Cord: Dextrose Ringer Phosphate	Tissue Analyses for Sugar and Lactic Acid: Blood, Mg. per 100 Cc.: Sugar	Blood, Mg. per 100 Cc.: Lactic Acid	Spinal Fluid, Mg. per 100 Cc.: Sugar	Spinal Fluid, Mg. per 100 Cc.: Lactic Acid	Brain Tissue Mg. per 100 Gm. Wet Weight: Sugar	Brain Tissue Mg. per 100 Gm. Wet Weight: Lactic Acid	Spinal Cord Mg. per 100 Gm. Wet Weight: Sugar	Spinal Cord Mg. per 100 Gm. Wet Weight: Lactic Acid	Two Hour Oxygen Consumption, Mm. Oxygen per Mg. Wet Weight: Plain Ringer Phosphate p_H 7.4—37.5 C.: Brain	Plain Ringer Phosphate p_H 7.4—37.5 C.: Spinal Cord	2 per Cent Dextrose Ringer Phosphate p_H 7.4—37.5 C.: Brain	2 per Cent Dextrose Ringer Phosphate p_H 7.4—37.5 C.: Spinal Cord
Normal.....	1 (ether, 4/10).....	0.98	0.99	0.98	1.00	193.0	86.6	75.0	26.8	99.0	151.0	27.8	94.0	1.64	0.30	2.18	0.53
	2 (ether, 5/11).....	....	....	1.00	1.00	233.0	195.9	59.0	12.0	26.4	162.0	42.0	90.5	....	0.27	....	0.50
Poliomyelitic	3 (ether, 3/13).....	1.03	1.00	0.93	1.03	.....	....	....	....	68.0	122.0	....	....	1.30	0.23	1.84	0.28
	4 (3/23).....	1.10	1.00	1.00 0.93	1.00 0.95	148.0	19.2	....	....	51.5	84.5	....	106.0	1.37	0.29	1.65	0.46
	5.....	....	....	....	....	272.0	....	119.0	28.3	83.3	122.5	68.7	84.5				
	6 (5/1).....	....	....	1.08 gray matter only	1.09 gray matter only	78.0	15.4	....	....	40.0	125.0	33.5	93.0	....	0.59*	....	0.58*
	7 (5/19).....	....	....	....	....	100.0	36.3	....	....	41.0	136.0	52.5	72.0				
	8 (5/28).....	....	....	....	....	136.0	42.0	68.0	10.0	59.8	85.0	65.0	55.0				

* Spinal cord, gray matter only.

In animals experimentally infected by intracerebral inoculation with poliomyelitis virus no change from the normal respiratory quotient of unity was found for the tissue of the cortex of the brain.

The lactic acid content of the spinal fluid, brain and spinal cord was found to be similar to that of normal control animals.

In measuring the respiratory quotient of spinal cord in normal monkeys the quotient of unity was again obtained. The minced whole cord of poliomyelitic monkeys in plain Ringer's phosphate solution gave readings of 0.93 in two experiments and quotients of unity in two other experiments. Both specimens in 0.2 per cent dextrose Ringer's phosphate solution gave a respiratory quotient of unity, indicating the ability of poliomyelitic cord (also of normal tissue from the spinal cord) to oxidize dextrose. We are continuing these experiments on the determination of the respiratory metabolism of the anterior gray matter of the spinal cord in experimental poliomyelitis. One group of determinations of gray matter from the anterior horn taken from the paralyzed segment of the cord of an animal with poliomyelitis gave a respiratory quotient of 1.08.

Himwich [25] has shown that the tissue of the brain may remove or add lactic acid to the blood under different conditions. Studies by Osnato and Killian [27] on the lactic acid content of cerebrospinal fluid showed that lactic acid was increased in the fluid in cases of septic meningitis and in epilepsy directly after a motor seizure. They reported cases of epidemic encephalitis and polioencephalitis with normal content of lactic acid in the spinal fluid. There is apparently no change from the normal lactic acid content in spinal fluids in animals with experimental poliomyelitis.

Peters [28] has shown recently that in polyneuritic pigeons with a deficiency of vitamin B_1 the ability of the brain tissue to oxidize lactic acid is diminished. Himwich has confirmed this work and demonstrated a respiratory quotient of 0.89 in the brain tissue of animals with B_1 avitaminosis (i. e., instead of 1.0 in normal animals).

The addition of dextrose to the immersion fluid increases the respiratory metabolism of minced normal and poliomyelitic spinal cord and brain tissue. In the same medium the oxygen consumption of minced poliomyelitic spinal cord shows a slightly diminished intake of oxygen in both plain and dextrose Ringer's phosphate over a two hour period (two animals) as compared with two normal animals.

Two experiments on minced spinal cord (white and gray matter) of poliomyelitic monkeys in the acute stage yielded slightly depressed

27. Osnato, M., and Killian, J. A.: Significant Chemical Changes in the Spinal Fluid in Meningitis with Special Reference to Lactic Acid Content, Arch. Neurol. & Psychiat. **15**:738 (June) 1926.

28. Peters, R. A., and Sinclair, H.: Biochem. J. **27**:1677, 1933.

respiratory quotients. It is evident that the injured tissue, although capable of producing gross clinical effects (i. e., paralysis), is not completely injured in its ability to oxidize some foodstuffs utilized by like normal tissue. On the other hand, since minced whole cord was used, it is possible that sufficient normal tissue may have been included to permit normal oxidations in the experiments performed.

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PSYCHOGENIC MOTOR DISTURBANCES

AN ANALYSIS OF THEIR ETIOLOGY AND MANNER OF DEVELOPMENT

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One of the most significant features in the present-day attitude toward motor disturbances is the gradual emancipation from the time-honored "organic-functional" dualism. For a long time, if even now one is entirely justified in using the past tense, the investigations in this phase of neuropsychiatry have centered about the arbitrary cleavage between the two components of this branch of medicine, the main efforts being concentrated on the detailed descriptive analysis of the symptoms characteristic of the one or the other. Tics, tremors, convulsions and the various forms of dyskinesias and akinesias have been associated in the mind of the physician with the one outstanding problem —that of the differentiation between the functional and the organic or between the domain of the psychiatrist and that of the neurologist. Paradoxically, the investigations that were undertaken primarily for the purpose of affording a clearer conception of these differentiations have resulted in a gradual tendency toward decreasing rather than accentuating the differences between the two. The recent discoveries of the influence exerted on the motor functions by the extrapyramidal and autonomic systems, discoveries that were particularly enhanced by the experiences with encephalitis epidemica and its sequelae, have shaken faith in the possibility as well as the desirability of a clearcut demarcation between the physical and mental components. On the one hand, the investigations of neuropathologists and physiologists have shown that disturbances in movement which have hitherto not been considered to be due to organic lesions are definitely associated with them. In addition to this it was discovered that in a large number of the organic disturbances some of the symptoms could be traced back to functional superimpositions developing on the basis of psychologic mechanisms in the course of the patient's adjustment to the organic lesion. On the other hand, even the most enthusiastic of the proponents of psychogenic determination of certain types of motor disturbances have come to see that it is possible that in most psychogenic disturbances pathophysiologic involvements of the tissue may be present. For even if a certain form of hypokinesia, for instance, could be justifiably considered

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as caused by psychic experiences in the life of the individual patient, it is possible and even advisable to assume that these factors may be associated with, or causative of, certain disturbances in the physiology of the tissues of the central nervous system related to these functions. Investigations along the lines of action currents, chronaxia and response to drugs and to other stimuli of the vegetative nervous system have shown the existence of such physiologic changes in association with definitely established psychogenic motor disturbances.

The appreciation of these facts has resulted in a definite change in the manner of approach to this and allied problems. First, the rigid differentiation between functional and organic disturbances, in which the diagnosis of the one automatically excluded the other, has been supplanted by a more plastic attitude in which one speaks in terms of a predominance of the one or the other. Secondly, for a better appreciation of the most advisable methods of treatment, the center of interest has shifted from attempts at a descriptive isolation of symptoms to an investigation of the dynamics of etiology and pathogenesis. It is with these considerations in mind that in the present communication an attempt will be made to present the various possibilities in the manner of development of psychogenic motor disturbances. It must be emphasized, however, that the term psychogenic refers primarily to considerations of causative factors and is not to be understood as an indication of the absence of pathophysiologic changes.

Whatever the differences between the various theories concerning the development of these symptoms may be, they have this in common: they recognize a certain purposive element in these disturbances; that is, they usually subserve some need of replacing one form of adjustment by another. Consequently, the following general concepts have at different times presented themselves to different observers as etiologic possibilities.

1. *Conscious Motivation.*—That such symptoms as psychoneurotic convulsions, paralyses and disturbances in gait have frequently been found to serve the purpose of gaining for the patient an escape from an intolerable situation makes it logical to suppose that, in some cases at least, the person who manifested these disturbances assumed them consciously for the purpose of gaining that end.

2. *Imitation.*—The fact that in a large number of cases psychogenic motor disturbances developed in connection with the observation, by the patient, of other persons with similar disturbances; the fact that in some instances when a disturbance of this type, whether on an organic or a psychogenic basis, has developed in one person it has afterward tended to spread from this person to others around him, sometimes in the nature of an epidemic, and finally, the fact that a large number of

patients in whom the absence of certain types of organic lesions could be definitely established have shown movements more or less exactly simulating those that would be caused by such organic factors have been used as indications that such factors as imitation or strong suggestion were of prime importance in the development of these disturbances.

3. *Conditioning.*—The important discoveries in the field of conditioned reflexes by Pavlov and his associates and followers have shown how indifferent stimuli which happen to affect an organism in association with important and specific instinctive experiences may in themselves become expressions of the latter. Whether purposely or accidentally established, such specific reactions to indifferent stimuli may later become part of the physiologic function of that organism. It thus seemed possible that a large number of the psychogenic motor disturbances which in particular persons appear to be expressive of certain emotional drives may have been established on the basis of conditioning.

4. *Psychologic Mechanisms.*—Within recent years, especially since the epoch-making investigations of the psychoanalytic school, it has become apparent that in a large number of disturbances of this type a definite relationship could be seen to exist between certain thwarted instinctive expressions and the disturbances that manifest themselves in the disease. It is important here to appreciate the difference between this concept and that of conditioned reflexes. In the first, one deals with relationships established on the basis of logically conceived reasons, among which in the vast multitude of possible conditioning factors and symptoms there is a choice of one or several particular ones that are determined by such a relationship. In the second, one deals with primarily nonspecific or even accidental connections in which the person simply follows the physiologic tendency to combine two conditioning factors which happen to occur at the same time.

In investigations of individual cases one finds most frequently that not one but several of these possible forms of causative mechanisms are at work. An analysis of the following cases is presented as indicative of such a combination. As one undertakes a deeper study of the special settings in which these disturbances occur and the histories of the persons who manifest them, one finds first that, depending on the attitude of the observer and the particular causes for which he is searching, reasons can be found for the assumption that any one of the aforementioned is the predominant or even the only factor. But with an unprejudiced approach one will find that in no instance can a single factor be justifiably taken as the only cause of the disturbance, but that a combination of factors belonging to the different categories enumerated earlier is instrumental in bringing about the disturbance.

REPORT OF CASES

CASE 1.—A white American girl, aged 13, was referred to the hospital with the history that for about four years she had been showing peculiar ticlike movements, accompanied by the utterance of certain words. It was stated that the condition developed shortly after the patient was frightened by a bull. There was no actual injury, but shortly after the experience she began to show these movements. She would twist the body, throw the head backward, jerking the legs and make facial grimaces. With these movements there would occur a compulsive repetition of words of a vulgar character. This occurred at first only at long intervals, but became more frequent as time went on and did not seem to depend on the patient's knowledge of being observed by any one. She stated that she did not appreciate saying the words and that the movements, although she knew of them, were of a compulsive nature, and that she was unable to control them. The history showed that the mother was considered to be high-strung and nervous, and that one paternal uncle had epilepsy. The girl was born on a farm and, except for the usual children's diseases, did not have any serious illnesses. The father was quick-tempered and rather sharp with the children; the mother, neurotic and somewhat indulgent. The patient's only sibling was a brother, about nine years her senior, to whom she was much attached; however, she had always had many quarrels with him. She started school at the age of 6 and showed a normal intellectual development. She had been well until four years before admission, but after that, with the development of the symptoms, showed an increasing nervousness, distractibility and a tendency to day-dreaming and confabulation.

An analysis brought out the following important factors: The earliest memories were those of the strict attitude of the father, who had frequently whipped her, one particular time at the age of 18 months for doing "something bad." Although the memory was vivid in the patient's mind, she was not able to remember the particular details of her own misbehavior, and no other information was obtained concerning this. At the age of 4 the patient was forced into sexual intercourse by a boy seven years older. Although she did not at the time appreciate the meaning of this occurrence, she was emotionally wrought up over it. She did not discuss it with any one. At the age of 7, shortly after entrance to school, she began a friendship with a girl somewhat older than herself who began to discuss with her associations with boys, and at one time invited the patient to accompany her and two older boys in sexual play. In describing this activity the older girl used the colloquial term for sexual intercourse, and when the patient did not understand the meaning of the term, the girl described it; it was immediately associated in the patient's mind with her experience at the age of 4. The patient became frightened, refused to go with her friend and ran home to tell her mother. The mother, who has always been prudish about sexual matters, spoke to the patient in emphatic terms instructing her never to think about such matters, certainly "never to do anything like that as it will ruin you for life." She was particularly upset about the patient's repetition of the terms used by the other girl, stating to her that it was as much a sin to pronounce these words as it was to indulge in these activities (it was at this stage in the analysis that the patient indicated her realization of the fact that these were the words she used during her nervous spells).

The girl apparently brooded a great deal over these matters and shortly afterward approached the mother for an explanation of the nature and necessity of sexual activities. The mother appeared ill at ease and was rather vague in her description, but mentioned as an analogy the activities of the farm animals. To the little girl the entire procedure appeared in the nature of a physical assault

and she became frightened, but at the same time thought about her own experiences at the age of 4. When the father found her watching these activities, he reprimanded her sharply and told her to run home and never to engage in such observations again. At this time, too, she saw a person who was brought in from the farm seriously wounded by a bull. The fear connected with this experience was again associated with the observation of sexual activities that she had made earlier. It was shortly after that and just before the development of the present condition that the patient was taken by her mother to see a man who was suffering from some form of nervous disease characterized by jerkings of the arms and head and peculiar facial grimaces. The patient was fascinated by this experience and requested the mother to explain the cause of such a disease. The mother was somewhat vague about it herself, but stated that, according to the history, it came from a bad fright, but that she thought it was possibly connected with some sexual promiscuity. It was a few days after that that the patient on her return home had to cross the place where the cattle were kept. The gate was open and she saw a bull pawing the ground and acting as if he were to charge at some one. In describing this the patient volunteered the statement that the bull acted in a fashion similar to that which she observed in the animals in the process of mating. The animal came out through the gate, and the patient became frightened and ran home with the animal running after her. When she came out of the state of panic at home she began to think about the man she had seen and began to wonder whether she herself would not acquire the same type of disease. Paramount in her mind as the reasons for such a possibility were her sexual delinquency and the fact that she was frightened. She began to watch herself for the appearance of such symptoms and spent a great deal of time standing in front of a mirror watching herself, and at the same time going through the performances which she remembered observing in the man. While she did this, she found herself thinking of her early sexual experience and also of the associations with the older girl who had asked her to go out with the boys.

Running parallel to these experiences were the associations with her brother. She was much attached to him, and as they were the only children in the home, he used to pay a great deal of attention to her, taking her to shows with him and in a playful fashion telling her that she was "his girl." She associated this relationship with the stories told her by her girl friend, but at the same time felt that she was justified in going with him and allowing him to be affectionate with her because he was her brother. Shortly before the onset of the present illness the brother, who at that time had reached the age of 18, began to go out with girls of his own age and the patient became jealous. Her attempts to win back his attention were not successful, and she brooded a great deal over her failure to do so. The thought that her brother was going out with other girls and not paying any attention to her seemed to aggravate the nervousness and the jerkings. About two and one-half years before her admission to the hospital, the brother, who at that time had need of money and knew that the patient had saved the amount necessary, suggested that she loan it to him, and agreed to give up his associations with the other girls if she gave it to him. She did so, and for a while her brother's attentions seemed to alleviate her nervousness a great deal. Soon, however, he began to neglect her; at the same time he made her realize that she was not going to get the money back. With that the twitchings and the nervousness came back; in fact, they became more pronounced than before, and a further exaggeration in the symptoms occurred when the brother married. After that the patient became depressed and refused to take interest in any activities; the jerking spells became more frequent, and the compulsive words accompanying them became more numerous and intense.

The analysis succeeded not only in giving the girl an appreciation of the mechanisms of the development of her condition but also in removing the symptoms. She returned home and has been well since.

The factors obtained through analysis of this patient show clearly the various factors that have combined in producing the motor disturbance, as well as the compulsive utterings. One can see primarily that throughout the chain of symptoms there runs a thread of definite purpose. Just how many of the acts and words were really consciously appreciated by the patient without outsiders being aware is a question which cannot be settled. Even after the conclusion of the treatment the patient insisted that she could not at the time remember the nature of the words that she said or the thoughts that she had while going through the movements. It is possible that a certain degree of malingering was present, especially in regard to winning back the affection and interest of the brother. As a fact, the incident of the brother's borrowing the money and not repaying it was on various previous occasions given by the patient as a cause for the exaggeration of her symptoms. One is justified in assuming, therefore, that to a certain extent she used this as a weapon in a conscious manner to obtain what she wanted from her brother. In addition, one finds a clear example in this case of the element of imitation as causative of the particular movements that the patient showed. It is clear that the pattern of her twistings and jerkings was studiously and almost purposively copied from the man whom she saw just before the onset of the present condition. It must be emphasized here, however, that at no time before the analysis did the patient show any appreciation of the fact that her movements were imitations of this condition; she thought rather that in her they were caused by the factors that she was told were instrumental in the case she saw.

One sees, however, that underlying both of these rather superficial mechanisms there were deeper ones that had prepared the soil, so to speak, on which the other two were engrafted. The most easily accessible of them was the accidental conditioning, in which a relationship was established in the mind of the patient between sexual activities and physical danger, between such activities in human beings and those in certain types of animals, between the frightening effect of the rage of the animal and the development of the disease and, finally, between the disease and sexual activities in general. As one goes deeper into the analysis of the case one finds in another substratum the psychologic mechanisms by which relationships were established between sex relations and the ideas of guilt and punishment, with the sensations of pleasure and a certain interest in them at the same time. This case furthermore shows the intricate interrelationships of numerous events and causes, all of which converge on the single clinical picture seen in the patient at the time when the disease was fully developed. The same

relationships, but possibly even more deeply and intricately related, can be seen in the following case.

CASE 2.[1]—A single, white, American girl, aged 22, was admitted to the hospital with symptoms pointing to an acute inflammation of the appendix, which had developed shortly after a friend had had an acute attack of appendicitis which resulted in the removal of the appendix. Although in this case the symptoms were not altogether pathognomonic, the appendix was removed. Immediately after the patient recovered from the anesthetic, there developed a series of abnormal movements which at the time were diagnosed as chorea. Under observation, however, it was noticed that the movements were not altogether characteristic of true chorea, and at the same time a number of other symptoms suggested the possibility of a psychogenic form of motor disturbance; an analysis was undertaken, which resulted in the disappearance of the symptoms. The following factors were discovered: The girl had lived with her parents until the age of 5, when her father died and she was removed to an orphan asylum. The patient was much attached to her father, for he had taken a great deal of interest in her. The analysis brought out the fact that her earliest memories were associated with two special types of activities with the father. The girl had had enuresis during her early years at home, and the father attempted to break her of the habit by a method which alternated between punishing her by spanking if she wet the bed and waking her up in the middle of the night and spending a great deal of time with her trying to get her to urinate before she was taken back. During such nightly sessions, in his anxiety to do all he could for her, he was indulgent and affectionate. He succeeded in making the patient enjoy these experiences so much that she did not want to cut them short, and therefore voluntarily held back the urine. The attempts to break her of the habit only made it worse, and it persisted until after she came to the orphan asylum. During the day the father, who was a butcher, used to take her to his shop, and she would watch him at his activities, pictures of which persisted in her mind as she grew up.

The enuresis continued for some time after she came to the orphan asylum, but as she failed to receive the interest that she had received from her father, she gradually gave up the habit. With the advent of puberty she began to feel definitely attracted by boys, but she remained shy and prudish on the surface. She spent a great deal of time fantasying contacts with boys, wherein she always imagined her mate as older than herself and as punishing and hurting her; at the same time he was affectionate toward her. Outwardly she failed to form any manifest attachments and was considered by the boys as standoffish and unsociable. When she was about 14, the inmates of the home were taken on a picnic. It was at this time that stories of "Jack the Ripper" were being circulated, and as the girls went to a picnic ground that was some distance from town, they talked a great deal about the possibility that some of them might be attacked by him. The patient did not take part in the discussion but listened attentively. On the trip back on the train she fell asleep. While the train was still in motion she suddenly woke up with a scream and in a pronouncedly excited state in which she threw her arms and legs about in a series of peculiar motions. She screamed and appeared to be frightened. When she finally became more tractable she explained that she had had a dream in which she was attacked by Jack the Ripper and that he had

1. This patient was observed in the neurologic service of Mount Sinai Hospital, New York. Dr. I. Strauss, chief of the service, and Dr. J. Turner, director of the hospital, permitted me to use the material.

stuck a knife in her abdomen. The movements persisted, and she was taken to a clinic where the case was diagnosed as chorea, and drugs and rest in bed were prescribed. The movements gradually disappeared after several months and did not reappear until the present attack. She continued to be nervous and easily upset, however, and two years later had an attack in which she was unable to pass urine and had to be catheterized.

She was discharged from the asylum at about the age of 19 and went to work in an office. She showed a good intellectual grasp of her work, but in her relationship to people in general, and especially to men, she remained shy and prudish, although she continued her fantasies, as already described. The descriptions that were obtained from the asylum were to the effect that the patient was always sensitive and rather sullen in disposition, but intellectually normal. A short time before the development of the pain in the right side she became acquainted with a young man, who began to show a great deal of attention to her. Contrary to her previous attitude toward men, she gradually began to draw out of her shell; an attachment for the boy developed, and she became engaged to him. Her painful symptoms first began when the boy, after their engagement, began to make more intimate approaches to her. With the development of the pain she began to lose interest in the man, expressing disapproval of his behavior toward her; she finally broke the engagement. The first appearance of the pain, as already stated, followed her actual experience with a case of appendicitis. As soon as the pain developed she began to think that she, too, had appendicitis and went to various physicians telling them that she needed an operation for the removal of the appendix. In recounting her experiences after the operation she stated that when she came out of the anesthesia and looked at the person who was engaged in putting the dressings on the wound, she had the same feeling that she had when she was coming back from the picnic; that is, she thought she had been attacked by Jack the Ripper. She stated that the movements were actually the direct sequel of her fight against Jack the Ripper in trying to ward off the attack.

In this case, too, one can see a number of mechanisms at work in the development of the symptoms. How many of them there were and to what extent they were consciously motivated remain unknown. There seemed to be little doubt concerning the actual unawareness of the patient of the causes leading up to the motor disturbance. The abdominal pain and its connection with appendicitis were probably nearer to the surface than the other symptoms. There seemed to be a definite purposive element in her insistence on the diagnosis of appendicitis and the necessity for an operation. It is evident, however, that the first indications of the symptoms followed the attack which she observed in her friend. Whether consciously or unconsciously, she therefore used the pattern suggested by this experience in the development of the symptoms that led to the operation. Beyond that one deals with phenomena that were not consciously appreciated by the patient before the conclusion of the analysis. The facts obtained by the analytic procedure leave no doubt as to the nature of the mechanisms that led to the development of the motor disturbance. First, one finds a definite series of conditioning processes that have resulted in the combination of various factors. Thus, one sees that the father's exaggerated interest

in her, especially in relationship to the enuresis by virtue of which she could obtain and hold the attention she desired, conditioned a certain pattern of gratification related to the urinary apparatus. The father's occupation, which remained so vividly impressed on the mind of the patient, and his punishment of her during his attempt to break her of the enuresis further conditioned the fixation of sadistic experiences in association with genital gratification. These conditioning influences could be followed, as they repeatedly manifested themselves in her fantasy life, in her fear of heterosexual associations, and in her reactions in the form of the two episodes of motor disturbances. Finally, running through the entire history of the patient, one finds a certain type of personality, sensitive, shy and introverted, with an instinctive drive easily subject to the development of abnormal forms of gratification. Throughout her life one finds a steady construction of a certain attitude toward sex, in which urethral and sadistic components replace the heterosexual form, and in her search for a substitute for instinctive gratifications, which were rendered unsatisfactory by constitution as well as experience, there is a constant revivification of a reaching out for sadistic expression. At the first manifestation of the motor disturbances there was in the dream a wish fantasy in which sexual cravings were satisfied by an injury to the abdomen, the movements (judging by those observed in the second episode) being a combination of sexual and defense components. The incident, which at that time had taken place in a dream, is then reenacted in real life through the medium of appendectomy, and the earlier pattern of disturbed movements reappears in reaction to this.

Similar occurrences with the same underlying mechanisms can be found with other psychoneurotic motor disturbances. Thus, for instance, one observes them frequently in cases of paralysis. The following case is typical of such a development.

CASE 3.—A married white woman, aged 45, was admitted to the hospital because of tremor of the right hand and paresis of the right arm and leg. In addition, she complained of double vision, numbness of the right side and occasional vomiting. There was no frank mental disease in the family. The father, an intelligent farmer and hard worker, was irritable, emotional and strict with his children; he punished them severely and managed the family entirely according to his whims. The mother died of diabetes shortly before the onset of the patient's illness; she had had three "strokes" and right-sided hemiplegia and anesthesia, making it necessary for the patient to take care of her.

The patient was the fifth of seven children, four of whom had various complaints of nervousness. She had had a year of college education and had taken training as a practical nurse. During childhood she was frequently punished by her father. He was opposed to her going to school, and during the first year he made school unpleasant for her by asking for a recitation of her lessons and punishing her severely when she made the slightest mistake. At the age of 18, she became interested in a young minister. The father objected to him as being above her class and forced her to marry a farmer so that she would remain near home. The

husband was as ill-tempered and coarse with her as her father had been. She tried to run away from him and return to her home, but the father forced her to go back. She had several miscarriages during the six years of marriage, and finally secured a divorce on the grounds of unfaithfulness. Two years later she married a meek, unassuming man who was the exact opposite of her father and her first husband. In 1929 she was in a car accident in which she was rather badly jarred. Four months later she began to complain of weakness and cramps in the right leg; paralysis of the right arm, double vision of the right eye and right-sided anesthesia, which were the chief complaints on admission, developed. Examination also revealed concentric contraction of the field of vision on the right. The intelligence quotient was 91. There were no signs of organic disease. During the treatment, in which hypnosis with catharsis and subsequent exploration were used, the following facts were obtained:

When, at the age of 6, she made her first attempt at studying, her father was extremely critical of her and punished her by slapping her right hand when she attempted to do a writing exercise under his supervision. She admired her father for his success and was much attached to him, yet a marked resentment developed against him because of his interference with her ambitions to attain an education. This resentment became more marked when the father interfered with her love affair and forced her to marry another man. The climax of this resentment was reached when, on the day preceding her marriage, the father, under the pretense of wanting to instruct her in marital affairs, exposed himself to her and requested incestuous relations. She told her mother, who warned her never to speak about it because of the scandal it would cause. For this reason the patient tried to forget the entire matter, and it was never mentioned again until the mother on her death bed, shortly after the occurrence of the paralysis, reminded her of it, making her promise that she would keep it a secret. The failure of the forced marriage increased the resentment against the father. The separation from the father during the second marriage relieved the situation somewhat, but the strain was introduced again when the mother's disease made it necessary for the patient to come back to the parental home. The father was critical about her way of managing her mother's condition and interfered frequently when she had to bandage the mother's paralyzed extremity. Shortly before the mother's death, the father requested that the patient take care of him after the mother's death, and the mother reenforced this with her pleas. It was at this time that the accident occurred, and the patient was slightly bruised about the right shoulder. The possibility of insurance compensation was taken up, but the result of the accident was considered as negligible. A few weeks after that, the mother died; the patient temporarily returned to her own home and tried to postpone moving to that of her father. Finally her father came to induce her to make the move. When she met him at the station she had been talking with a young man from the neighborhood to whom she felt some attraction; the greeting when they parted was rather warm. The father, noticing it, immediately reproached her in his old manner, crudely accusing her of being immoral. In that moment the strong resentment and hatred which had developed in the patient reached a climax, and she felt tempted to slap her father in the face. She had a strong feeling of guilt, and the phrase came to her mind that "the hand that is raised against the father shall wither away." Immediately she felt a shaking in the arm and an increasing weakness, which rapidly extended into the leg. She considered herself as stricken by the Lord. This made it impossible for her to go to help her father, as she became an invalid who needed medical care. While these memories were brought out by the patient, she realized the emotional factors which had contributed to the development of the paralysis, and the symptoms disappeared.

Here, too, one finds a similar multiplicity of causative factors in the production of the symptoms. There is no doubt as to the relationship of the pattern of right-sided weakness and numbness to the condition which she observed in the mother. Similarly, it was evident that financial difficulties were responsible for a consciously motivated attempt to make as much as possible of this weakness in order to procure compensation. Fundamentally, however, both of these mechanisms depended on her experiences preceding the accident and the special set of relationships that were built up in regard to her father and her sexual life in general.

In the first case there was noted the intimate relationship that may exist between hysterical disturbances in movement and obsessional forms of thought and activity. In a number of cases one finds the development of motor disturbances on the basis of obsessional symptoms, in which again one can see the same mechanisms at work, only they are usually secondary to the development of the obsessional symptoms. There are well known cases in which compulsive thoughts are expressed in certain fixed patterns of motion which the patient performs in an automatic fashion and the compulsive nature of which he becomes aware of only if the carrying out of these acts or movements is interfered with in some way. The stiff, awkward posture in which the patient with the hand-washing obsession holds his hands away from his body and from objects outside of him is a well known manifestation of such a disturbance. The ceremonial procedures, such as stepping out in a certain fashion in walking, holding one's hands or fingers in a particular fixed position, arranging the bedclothes according to a certain ritual, and buttoning and unbuttoning one's clothes in a certain fixed manner on particular occasions, are further manifestations of peculiar movements which develop on the basis of obsessive thought. The following cases are illustrative of the manner of development of activities of this type.

CASE 4.—A boy, aged 16, came to the hospital with the complaint of compulsive phenomena and obsessions that had existed for about two years. In the first interview he spoke of suffering from immoral thoughts that intruded themselves on his mind, these being in the nature of having "bad wishes" against his parents and in relation to certain types of men. Whenever he thought of his father, the thought that he wished his father were dead intruded itself on his mind. He could not think of his mother without having at the same time to think of "bad words" of a sexual nature. When he looked at certain men the thought came into his mind that he would like to be "one" with them, and sometimes that he would like to be of "the same religion" as they were. In addition, at times he would have the compulsive thought of attempting to visualize these men without any clothing on and would be particularly attracted to their genitals. These thoughts, he stated, had existed for two years, and in his attempt to get rid of them he began to perform certain movements which he thought could distract his attention and take his mind off them. For instance, a movement with the hand lifted above the head and then carried through between himself and the men who would evoke

these thoughts, if repeated a number of times, would give him slight respite from the thoughts. The bad wishes against his father and mother were counteracted at times if he placed his hand on a table and remained in this posture for some time; at others, by stepping out with the right foot with his head thrust forward. When observed in the ward he was seen to go through numerous movements of this type, and these sometimes coalesced to produce the picture of a bizarre motor disturbance carried out in swift, jerky movements.

Under analysis it was discovered that all of the thoughts were definitely related to a series of experiences, some of which had occurred in his early childhood and others shortly before the onset of the illness. The patient, who was the youngest of a large number of siblings, all of whom were robust and well adjusted, had always been of a shy and retiring nature, a feature which was particluarly enhanced by a series of diseases during childhood that left him a physical weakling. He had always had a marked respect and admiration for his father but had also feared his strict and domineering attitude. He had always had a great attachment for his mother and looked up to her for affection and protection. From early childhood he had indulged in fantasies of wishing to be like his father, a wish which he felt could not come true because of his physical weakness. The analysis showed definitely that in the first place this attitude toward the parents had resulted in jealousy of the father, because of a wish to replace him in the affections of the mother and because of envy of the father's stronger make-up. The mechanisms of the "bad thoughts" in relation to the father were obvious, and the movements which he undertook to counteract them were apparently favorite gestures of the father himself. Shortly before the development of the present symptoms the boy was introduced into a number of homosexual experiences with older boys. Whether his willingness to take part in these activities was indicative of a constitutional defect in sexual make-up or of the relationship to his parents in early life remains a question. He did, however, from the beginning feel a certain amount of guilt and shame for carrying out these activities, but he knew that he could not help them, as he was definitely attracted to certain types of men. As the condition progressed, he began to think of this attraction in terms of physical forces, which in his imaginative mind were represented in the form of lines connecting him with these men whenever he looked at them. It was for the purpose of breaking through these lines that the cutting movements of the hand carried between himself and the men were undertaken and afterward carried out in a compulsive fashion.

In this case the abnormal movements were not primary expressions of underlying conflicts but seemed to be developed in an attempt at adjustment to the primary symptoms, that is, the obsessions. It must be appreciated, however, that even here the pattern selected is definitely related to the mechanisms responsible for the entire picture. Thus, the gestures employed to counteract the "bad thoughts" in relation to the patient's parents are not picked up at random but represent an actual compensation for such thoughts. In identifying himself with his father he removed the need to wish that his father were dead. Similarly, the thoughts in reference to the men who attracted him were counteracted by an attempt at actual severance of a physical contact with them. Another example of this type of relationship is shown in the following case.

CASE 5.—A white, American boy, aged 15, was brought to the hospital because of "nervous" spells, consisting of bizarre movements accompanied by the compulsive shouting of unintelligible words. The movements were of a complex nature: The patient jumped up, beat his chest with both fists, waved his arms about as if warding off an attack, brushed his clothes in a quick, jerky fashion and twisted the hips and legs. The words, at first unintelligible, revealed themselves after the analysis as condensations of such phrases as: "I am going to cut you," "No, don't do it," "We mustn't be dirty," "I did not know it was wrong," "I don't want to be robbed," etc. In the spells the movements and utterances occurred at the same time and were accompanied by states of fear and feelings of guilt.

The analysis brought to light a wealth of material which served as the basis of the disease. Only a few of the most important experiences can be recorded here. It was found first that, although the severe symptoms had lasted only eighteen months, the patient had had "jerky" spells before, and that these started at the age of 6. They followed a series of incidents in which threats and attempts at castration were made on the patient by a number of boys who wished to frighten him. The jerky movements that developed then clearly represented attempts to fight against the boys and were accompanied by the words referring to "cutting" and "robbing." A number of other psychosexual traumas, mainly in the nature of homosexual and masturbatory practices, contributed to exaggerating the symptoms and the feelings of guilt and fear. At the age of 12, the patient started to practice sexual activities with animals and from the beginning felt ashamed and afraid of discovery. When he noticed that some of the animal refuse adhered to his clothes he acquired the habit of brushing them by vigorous rubbing with his hands. These movements gradually became automatic and were woven into the original jerkings and defense movements. The utterings "We mustn't be dirty" and "I didn't know it was wrong" referred to the latter activities.

Thus it will be seen that in this case, too, the bizarre movements and unintelligible utterings were definitely related to the development of the compulsive thoughts and words and were associated with the experiences in the life of the patient.

COMMENT

An analysis of the material presented brings into the foreground a number of features which are particularly significant in view of their practical importance. First, in the development of these disturbances there are always a number of causative factors, all of which converge on the resultant syndrome. Second, these factors do not represent any single type of mechanism, but are manifestations of the different types that were discussed in the introduction. Thus one may find conscious motivation causing certain forms of reaction, which can also be traced back to unconscious instinctive urges. Similarly, psychopathologic phenomena develop on the basis of early conditioning but are precipitated through the medium of suggestion or imitation. Finally, in some cases all of these mechanisms are at work in the production of the symptom complex. It is of importance to appreciate that these different etiologic

factors do not simply coexist but can be shown to be definitely interrelated in such a fashion that the occurrence of one is made possible only by the preexistence of the others. In case 1, for instance, the movements were definitely established on the basis of imitation and, to a certain extent, were adhered to with a certain purpose in the mind of the patient. It is just as clear, however, that the dyskinesia that had been observed in the man was imitated by the patient primarily because it was related to experiences that occurred in her childhood and because it could thus gratify a definite need in her life. Similarly, the consciously motivated acts were undertaken for the purpose of securing her brother's attentions, but the need for these attentions was conditioned long before that. These features can also be found in the other cases reported here.

In attempts to understand these disturbances and to apply treatment for them one must appreciate that the interrelationship of the various components in their development is characterized by a certain mutual interdependence: Factors that are of more recent occurrence can best be understood in the light of past experiences, whereas the latter are sometimes most easily obtained through the medium of the former. When one considers that the more recent occurrences are also the more superficial and, therefore, most easily accessible, one can readily appreciate the value of an approach in which both types are looked on as of equal importance. In each of the disturbances one must bear in mind that the causative factors which belong to the groups of conscious motivation and imitation, being the most evident, do not necessarily exhaust all of the possibilities, and one should not consider an analysis completed just because a superficial relationship of this type has been discovered. Conditioning in early life and subconscious psychologic mechanisms, if they are more difficult to reach, are also more fundamental in their relationship to the personality of the patient. One should not, however, neglect the consideration of the precipitating influence of the first two mechanisms simply because they appear more superficial. They represent the climax of the pathologic development of the disturbance and therefore serve as useful guides in the search for the more fundamental factors.

ABSTRACT OF DISCUSSION

Dr. F. G. Ebaugh, Denver: Psychogenic motor disturbances comprise a common group of personality disorders. They are characterized by a number of common fundamental qualities. The essential uniting feature consists of the highly significant fact that, in spite of extensive clinical and laboratory investigations, organic lesions cannot be objectively demonstrated. Conflict is inevitable when medical thinking finds it so difficult to rid itself of a notion that the term functional is an embarrassing excuse for ignorance and that at some future time ultrachemical and ultramicroscopic discoveries will reveal mysteries heretofore unsolved. This may be true. However, recent advances in psychiatric knowledge

have given factual material which should dispel both despair and speculation with regard to so-called functional disorders. This factual material does not compel one to accept the physicochemical inadequacies of anatomicopathologic alterations in the tissue as the only satisfactory explanation for all of the developments within the human organism.

A systematic approach with psychobiologic methods of investigation has given ample—and, because of strict adherence to facts, incontestable—evidence of the rôle which psychogenic factors may play in the development and maintenance of somatic disturbances. Pavlov's work with animals and Krasnogorsky's experiments on children have established beyond a doubt the dependence of physiologic functioning on emotional factors. Dr. Meyer dispensed with dualistic and pseudomonistic trends by introducing into medicine the concept of the mentally integrated person in whom life expresses itself in the form of involuntary automatic functioning of various parts on a vegetative level and of more or less conscious, symbolizing overt or implicit performances of the organism as a whole on a psychobiologic level.

Dr. Malamud has given an excellent exposition of psychogenic motor disturbances indicative of dysfunctions of a total personality. Dr. Malamud has also indicated that psychogenic motor disturbances are best understood and treated, not per se, locally and detached from a consideration of the patient and situation, but by means of studying the patient in his entirety, with attention to his physical, emotional, intellectual, constitutional and environmental peculiarities. The cases presented clearly show the influence of major life situations, such as parent-child relationships, difficulties of emancipation and heterosexual development.

Dr. Malamud has wisely pointed out the significance of adopting a more plastic attitude regarding psychogenic disturbances and of shifting interest from methods of description to psychobiologic investigations, for the purpose of establishing common sense treatment, the method of treatment to be based on a fundamental understanding of the forces at work and especially of the underlying mechanism of substitution present in psychogenic motor disturbances.

In my clinical experience, I find three types of substitution: (1) substitution with a clear association of the symptom with a well remembered emotional situation; (2) substitution with no conscious association of the symptom with a well remembered emotional situation, and (3) substitution with no conscious association of the symptom with a suppressed forgotten emotional situation.

Freud described substitution as a process by which sums of emotion become transformed into physical manifestations. He assumed that the forgotten or repressed situation is always of a sexual nature. One finds psychogenic motor disturbances of all varieties developing from many varied situations, such as fright, a beating by a drunken husband, vocational and school failures and witnessing of a homicide, all of which have led to one of the three forms of substitution described.

Dr. Malamud has given an excellent paper, in which he has taken a well chosen point of view concerning the multiplicity of the causes of psychogenic motor disturbances suggesting that one should base a therapeutic approach on demonstrable facts concerning the forces at work and their origin, development and modifiability.

Dr. P. F. Schilder, New York: In Dr. Malamud's case I should stress the fact that the patient was a young girl with an organism which was inclined to give motor manifestations of the choreic type. The problem seems to center on the fact that a psyche which does not have expression in the entire body does not exist. The entire problem of psychophysiologic connections is a pseudoprob-

lem. There are no connections, but the psyche is always a psychophysiologic process which manifests itself in the various levels of integration. Dr. Malamud has justly emphasized that one should always consider the various levels of this integration.

One of the clearest expressions of this general principle can be found in motility of instinctive and primitive type. Psychologic problems are often reflected with clearness in the so-called extrapyramidal system. When extrapyramidal psychogenic manifestations are in the foreground, one often finds that the patient was badly integrated as to extrapyramidal motility before the psychic trauma occurred. I have seen striking cases of this kind which presented a picture resembling paralysis agitans.

The way in which postural reflexes appear in man is also dependent on the factors of personality and psychic attitude. Schaltenbrand considered many of the phenomena described by Goldstein and his co-workers as merely phychogenic. But there are no phenomena which are merely psychogenic or merely physiologic. No motor activity takes place without involving the total personality, and there is no manifestation of the personality which is not reflected in the motility. The contribution of Dr. Malamud is a valuable approach to this general problem.

Dr. B. R. Tucker, Richmond, Va.: In studying the psychic phenomena of the aura of epileptic persons, I came to the conclusion that some of these phenomena could be purely psychic and some organic. As a brief illustration, I had a case of a man aged 22 or 23 who had epilepsy and partial congenital hemiplegia. Just before his convulsions he would, if he could, walk to a chair or a bench; if he could not get to one he would simulate leaning on one. He put his hands down and raised his leg as if to put it on a box; then he moved his hand up and down. I saw him once while he was in this aura. A few seconds afterward he had a convulsion. He remembered the aura. I asked him what he was doing. He said he was putting his hand on a box and taking his knee up and putting it on the box. He felt as if he had a hammer in his right hand and as if he were pounding a nail in the box. He said that he could feel the hammer in his hand and his knee on the box. I traced the aura back to the fact that, although at the time of the aura he was unemployed, he had once nailed up boxes in a box factory. This apparent phenomenon, which was possibly due to an aura of organic epilepsy in a man with partial congenital hemiplegia, was therefore probably the pure desire complex of wanting reemployment of the kind that he had once had.

The entire matter is extremely complex, and I think that one fails to define mixed psychogenic and organic elements and to relate them to susceptibility even in certain parts of the brain.

Dr. William Malamud, Iowa City: I am grateful to Dr. Ebaugh for his discussion of my paper and for the suggestion that the basis of my approach is similar to Dr. Meyer's psychobiologic concept.

Dr. Schilder brought out clearly the point that I attempted to emphasize: i. e., that the terms psychogenic and organic are only relative, referring to a predominance of the one or the other element, without being mutually exclusive.

Dr. Schilder's suggestion that psychogenic choreiform movements are particularly common in young children is probably true, but such movements do occur in adolescent boys and girls and even in adults. One of my patients, a woman, aged 21, whom because of lack of time I could not mention in my discussion, showed a syndrome diagnosed as chorea.

MYELOTOMY OF THE COMMISSURE

A NEW METHOD OF TREATMENT FOR PAIN IN THE UPPER EXTREMITIES

TRACY J. PUTNAM, M.D.
BOSTON

The treatment for pain in the abdomen and legs by means of chordotomy is now a well established and satisfactory procedure. Pain in the upper cervical region and in the face can usually be relieved without severe resulting disability by sectioning the posterior roots. The treatment for pain in the arms and shoulders has, however, not been very satisfactory. Adequate sectioning of posterior roots leaves the upper extremity entirely useless, and it is difficult to perform a chordotomy high enough to control pain in the arms. It must have occurred to many neurologists that a patient with intractable pain in the arm or shoulder would be better off if he happened to acquire syringomyelia, and the suggestion has doubtless been made that artificial destruction of the pain fibers as they cross in the decussation about the central canal would be a rational procedure. As far as I know, it has never previously been attempted. I have carried out this procedure in three instances.

The first patient was a woman with carcinomatous metastases in both axillae, with extreme pain. The cord was exposed from the fourth cervical to the third dorsal segment, and a needle was inserted between the posterior columns at intervals of a few millimeters up and down the exposed area and maneuvered in such a way as to pass through the commissure. It was found possible to carry this procedure to a segment or two beyond the limits of the laminectomy. The patient was not upset by the operation and was completely relieved from pain until death two months later. She showed a loss of sensation to pin-prick approximately over the fifth to the eighth cervical segments but practically no loss of tactile or position sense (fig. 1). There was a certain amount of atrophy of the small muscles of the hands, but they were as useful as they had been before the operation. There was a loss of vibration sense in the legs, but no ataxia. The perception of pin-prick returned a week or two after the operation, but the spontaneous pain did not reappear.

Read at the Sixtieth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 4, 1934.

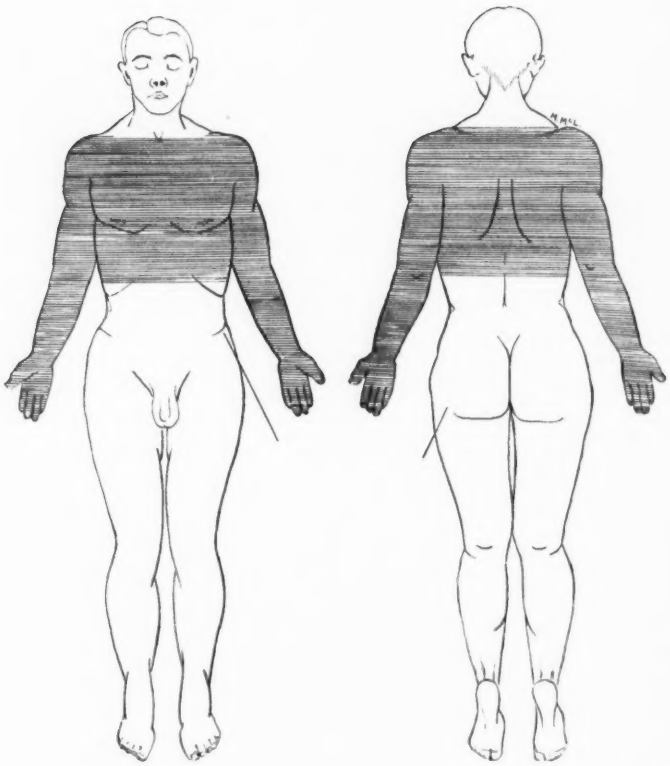

Fig. 1 (case 1).—Diagram showing the loss of sensation of pain following myelotomy of the commissure. There were no changes in the reflexes. The shaded areas represent the parts in which the sensations of pin-prick, heat and cold were lost while the sense of touch and that of position were unimpaired. The light areas show the parts in which the sense of vibration was lost and the sense of position was unimpaired.

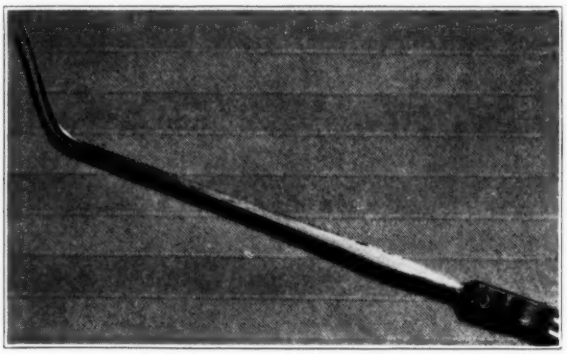

Fig. 2.—Special thin myelotome, which can be inserted between the posterior columns without cutting the posterior spinal vessels.

The second patient was a man with pain from carcinomatous metastases, apparently from the lung, which affected both sides of the neck as well as the axillae. The pain was so severe that doses of ¼ grain (0.016 Gm.) of morphine did not wholly relieve it. A procedure similar to that used in case 1 was carried out on this patient, except that a special instrument was used which appeared to give better results than the needle (fig. 2). In this case the section of the commissure was carried up to the first cervical segment. This patient showed no atrophy of the hands, but he was not completely relieved of pain in the upper cervical segments. The pain was, however, dull and burning

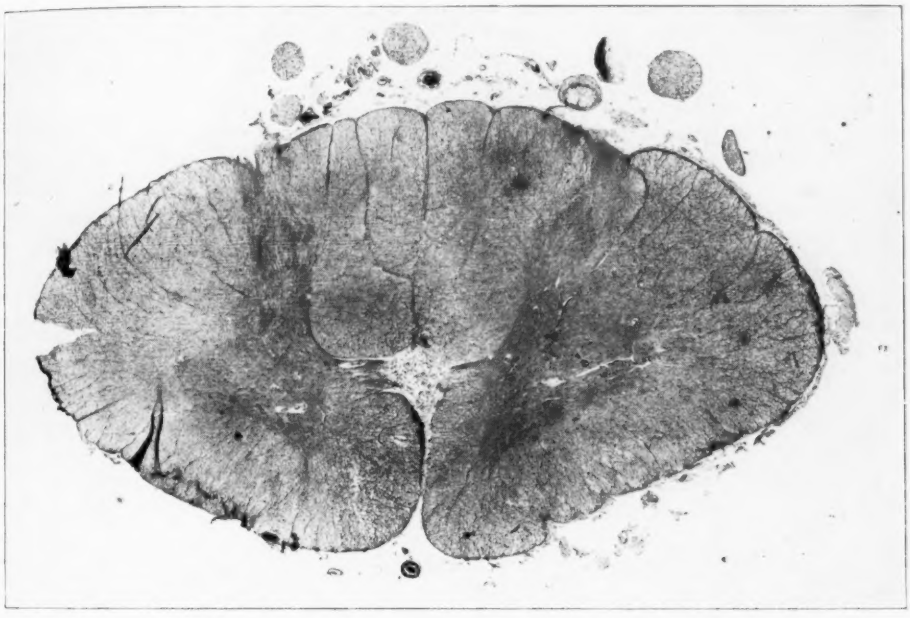

Fig. 3 (case 1).—Section of the cervical portion of the cord removed at autopsy two months after operation, showing the extent of the damage produced. The commissure is completely divided. There are practically no cells left in the posterior horn. At a few levels of the cord the area of destruction was larger, extending into the anterior horn or posterior columns. Neutral red; × 8.

instead of sharp, and codeine instead of morphine produced sufficient relief.

In the third case the operation ended fatally, and it doubtless represents an error in judgment as well as an error in technic. The patient was a cachectic old woman, almost moribund from carcinomatous metastases to the shoulders and neck. She died following an operation in which the commissure was divided through the entire cervical region and the first two dorsal segments. It is probably wiser not to section the poste-

rior roots in the segments above the fourth cervical segment on account of the possibility of respiratory difficulties.

Sections from the spinal cord in the first case showed very moderate damage to the posterior columns and a satisfactory division of the commissure throughout most of the extent subjected to operation (fig. 3). At a few levels the anterior horns were affected. The damage should be less with the new instrument.

This operation could be modified so as to affect only the posterior horns of one side if the incision were made ventral to the posterior roots. The precise indications for the operation remain to be established, but the procedure should, on the whole, be safer than a bilateral cervical chordotomy and should be free from the danger of paralysis of the bladder.

ABSTRACT OF DISCUSSION

Dr. Francis C. Grant, Philadelphia: I can present only a theoretical opinion on this procedure. It seems that by this operative technic anesthesia can be produced in selected sensory segments. Following chordotomy and section of the anterolateral bundles a horizontal or columnar desensitization to pain occurs in all the areas below the incision. By myelotomy a segmental or vertical analgesia is produced, the segments below not being involved.

Myelotomy must be compared with rhizotomy as well as with chordotomy. Rhizotomy is easier to perform, requires no larger laminectomy and has the advantage that, as the roots are cut outside the cord, damage to the tracts does not occur. But rhizotomy is accompanied by a loss of all forms of sensation. The cutting of all the posterior roots supplying sensation to a limb produces nearly complete uselessness of that extremity owing to a loss of positional and tactile sensation. Myelotomy obviates this disadvantage but carries with it dangers of injuring adjacent tracts through the incision into the cord. Furthermore, the loss of pain following myelotomy is bilateral, and relatively few patients have bilateral pain.

The merits and demerits of chordotomy are well understood. In experienced hands a unilateral chordotomy is a very satisfactory procedure. But chordotomy in the cervical region—and it is in this area that myelotomy seems most likely to be used as a substitute—carries with it a danger of phrenic involvement. However, myelotomy also has this disadvantage.

I should like to ask Dr. Putnam how many segments above and below those actually involved it is necessary to cut in order to be certain of affording relief. From his operative procedure it may be possible to determine whether or not pain fibers decussate at the level at which they enter the cord or whether they pass upward a segment or two before crossing.

Dr. Putnam has described how he avoids injuring the posterior spinal vessels. The chief difficulty in this procedure is in keeping exactly in the midline, thus preventing damage to adjacent fiber tracts. Fortunately the posterior columns are relatively unimportant and the pyramidal tracts so laterally placed that they should always escape injury.

In selected cases, especially if the pain is bilateral, myelotomy seems to have certain possibilities and advantages over existing procedures. However, further experience with this operation is needed before a definite opinion can be presented.

Dr. William G. Spiller, Philadelphia: I am deeply interested in all that pertains to chordotomy. A case which I reported in 1905 proved to me the exact

situation of the pain and temperature fibers in the spinal cord. A patient had much impairment of sensation for pain and temperature in the lower limbs while tactile sensation was preserved in these parts. A small tubercle was found in the right anterolateral column at the lower end of the thoracic portion of the cord, and another tubercle was found ½ inch (1.27 cm.) higher in the left anterolateral column.

I had heard complete transverse section of the spinal cord recommended for the relief of pain in the lower part of the body, and I believed that a segmental section of the tracts for pain and temperature should be sufficient for this purpose. So far as I could acertain, no one had ever performed a segmental section of the cord. I did not know what complications might arise from this; I thought that a severe intramedullary hemorrhage might be produced. I requested Dr. Martin to cut these sensory tracts in a patient of mine who had intense pain in the lower limbs caused by an infiltrative tumor of the cauda equina which had been found at operation. The sectioning of the sensory tracts was performed on Jan. 19, 1911, and the patient's condition improved, but I was afraid that the report of the case might lead to rash attempts to follow this example by surgeons not familiar with operations on the spinal cord. Therefore, the report was not published until May 18, 1912, sixteen months later.

The operation by Tietze and Foerster for gastric crises, performed in December 1912, was reported before a medical society on June 6, 1913, and the report was published on Aug. 11, 1913.

I am much interested in the suggestion offered by Dr. Putnam. It is stated that two of his three patients experienced relief following the operation. If the incision is made at the posterior septum it must cause a complete division of the two halves of the cord through a considerable distance. Evidently Dr. Putnam has not met with serious hemorrhage in performing this operation. I believe that it would be possible to divide the commissure through the anterior fissure and, possibly, to use a curved blade. This could probably be done without causing more hemorrhage than is produced by the posterior division. With either method hemorrhage from the artery of the anterior fissure might cause great damage to the nerve cells of the anterior horns. More than two cases are needed to judge the efficacy of this method.

Dr. Tracy J. Putnam, Boston: It takes far less courage and originality now to interfere with the tracts of the cord than it did when Professor Spiller first suggested the chordotomy. I believe that the procedure under consideration should be regarded as a subvariety of chordotomy rather than as an entirely new operation.

Bleeding has not been a very serious factor because of the fact that I have used a thin blade between the curves of the posterior spinal vessels.

One technical advantage of the operation is that a rather narrow laminectomy incision may be used. It is not necessary to expose the whole posterior aspect of the cord, and this means that the actual laminectomy itself is considerably easier. Of course, the incision has to be a good deal longer than for chordotomy. I believe that it should be reserved for instances in which there is pain in both upper extremities.

The resultant analgesia appeared to be about two segments narrower than the zone which was incised.

I might add one further technical point: By the use of a long instrument it is possible to run the incision in the cord beyond the limits of the laminectomy incision, and in this way the instrument can be pushed farther up and also farther down than the bony defect.

GRADUATED JUGULAR COMPRESSION IN THE LUMBAR MANOMETRIC TEST FOR SPINAL SUBARACHNOID BLOCK

WILLIAM T. GRANT, M.D.
AND
WILLIAM V. CONE, M.D.
MONTREAL, CANADA

The lumbar manometric test is a routine procedure whenever disease of the spinal cord is suspected. Stookey, Merwarth and Frantz [1] and Stookey and Klenke [2] have standardized the original test of Queckenstedt by introducing new procedures in it, greatly increasing its value. Their contributions consisted in adding touch compression of the jugular veins, timing and charting the rise and fall of pressure after firm jugular compression, and finally in emphasizing the value of Ayala's index, or what they called the pressure index.

Attention to a host of details which modify the pressure readings is still required, and the chief source of error is concerned with the maneuvers incident to manual jugular compression. Elsberg and Hare [3] introduced the amyl nitrite test for spinal subarachnoid block, because of the disadvantages of manual jugular compression. The amount of pressure on the jugular veins that is often necessary may cause the patient considerable discomfort. Many persons have a tendency to hold their breath or to strain during the period of compression and alter the cerebrospinal fluid pressure, thus leading to errors. In persons with stout necks it may be difficult to exert sufficient pressure on the jugular veins. In thin-necked patients the carotid arteries may be compressed somewhat or a sinus caroticus reflex may be set up. When assistants are not trained to locate the jugular vein accurately, the test cannot be satisfactorily carried out.

From the Department of Neurology and Neurosurgery, McGill University.

Read by title at the Sixtieth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 4, 5 and 6, 1934.

1. Stookey, B.; Merwarth, H., and Frantz, A.: Manometric Study of the Cerebrospinal Fluid in Suspected Spinal Cord Tumor, Surg., Gynec. & Obst. **41**: 429, 1925; Proc. A. Research Nerv. & Ment. Dis. **4**:185, 1924.

2. Stookey, B., and Klenke, D.: A Study of the Spinal Fluid Pressure in the Differential Diagnosis of Disease of the Spinal Cord, Arch. Neurol. & Psychiat. **20**:84 (July) 1928.

3. Elsberg, C., and Hare, C.: A New and Simplified Manometric Test for the Determination of Spinal Subarachnoid Block by Means of the Inhalation of Nitrite and Amyl, Bull. Neurol. Inst. New York **2**:347, 1932.

The amyl nitrite test eliminates many of the drawbacks of manual jugular compression but adds others. A few persons do not react to amyl nitrite. The average rise in spinal fluid pressure is not great, even in cases without block, being 162 mm. The rate of fall is normally too slow to be of value in any case. The test, they state, should not be repeated for at least one hour.

We have not been entirely satisfied with either manual jugular compression or the amyl nitrite method. For some time now, since the suggestion of one of us (W. G.), we have been using a sphygmomanometer with its cuff about the neck to block the venous return from the head. The most significant advantage is the fact that it allows a wide variety of measurable pressures with a corresponding range in the degree of obstruction to the venous return from the head. There is not the uncertainty associated with manual compression, and as a rule the patients do not mind the procedure and breathe regularly, even with the cuff pumped up to a pressure of 100 mm. of mercury. Very important too is the fact that the degree of pressure used can be accurately duplicated at will by the same or other observers. When the patient's systolic blood pressure is at a low level the higher pressures are unnecessary and can be dispensed with. There is much less possibility of a sinus caroticus reflex. Many readings at various pressures on the neck can be quickly taken without shifting the patient's position in any way. Before the lumbar puncture is done, an untrained assistant can be shown quickly how to carry out the jugular compression accurately with the manometer in place on the patient. This serves to accustom the patient to the procedure and assures his relaxation and cooperation.

PROCEDURE

An ordinary blood pressure cuff is wrapped loosely about the neck. It is then completely covered by several layers of gauze bandage to prevent undue expansion of the rubber bag and to decrease the amount of pumping required in its adjustment. If it is too tight it may obstruct the venous return somewhat so that the initial pressure is slightly raised, but it does not alter the character or magnitude of the responses. If it is too loose it means only that more pumping is required to obtain the desired pressure readings. The mercury manometer or a gage of the aneroid type is then attached to the cuff around the neck. The lumbar puncture is done and a spinal fluid manometer of the Ayer type attached. When the pressure has become stabilized the initial readings are taken and the oscillations due to respiration and pulse are recorded.

To compress the jugular veins the cuff is pumped up as rapidly as possible to the desired pressure and held there for ten seconds, and then the valve is released. It is first inflated till the gage registers 5 mm. of mercury and released after ten seconds. When the fluid in the manometer has come to rest the cuff is again pumped up, this time to 10 mm. The same procedure is repeated five times, using

cuff pressures of 20, 40, 60, 80 and 100 mm. On releasing the pressure in the cuff, manometric readings are made every ten seconds until the fluid level remains stationary.

RESULTS

Using the blood pressure cuff as outlined and employing the range of pressures between 5 and 100 mm. of mercury, one secures in a normal patient a graded series of responses as shown in chart 1 which was obtained during a routine lumbar puncture. The initial cerebrospinal

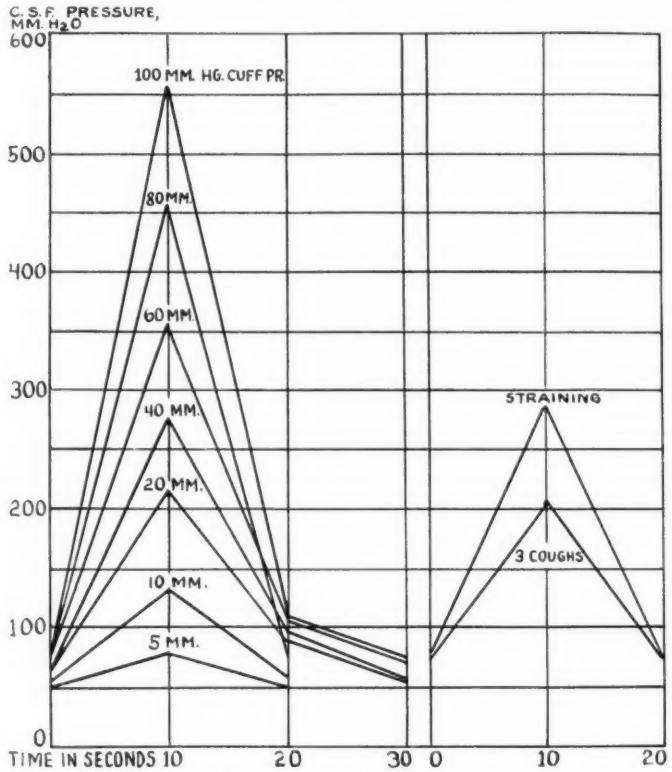

Chart 1.—Graph obtained in a patient with normal responses; the number on each line at its peak indicates the pressure of the cuff in millimeters of mercury. The initial cerebrospinal fluid pressure is 50 mm., and the responses in the cerebrospinal fluid pressure vary from 80 mm. of water at a cuff pressure ot 5 mm. of mercury to 550 mm. at a cuff pressure of 100 mm. In most patients who give presumably normal responses, the elevation following coughing and straining is considerably less than that resulting from the higher degrees of jugular compression.

fluid pressure was 50 mm. of water. With a pressure of 5 mm. of mercury in the cuff about the neck the cerebrospinal fluid pressure rose in ten seconds to 75 mm. of water. At a cuff pressure of 100 mm. of

mercury the cerebrospinal fluid pressure reached 550 mm. of water. The rate of rise in cerebrospinal fluid pressure is greater than the rate of fall, so that the curve tends to flatten out as the initial pressure is reached. This is more evident with the higher pressures and is less noticeable after coughing and straining. It is a constant finding and is not considered the result of incomplete relaxation on the part of the patient.

The changes in pressure seen in chart 2 are strikingly different and the summary of the case follows:

REPORT OF A CASE

The patient, aged 52, was admitted to the service of Dr. Harry Dolan at St. Mary's Hospital thirteen days after an undiagnosed fracture dislocation of the fifth cervical vertebra. He complained of numbness and weakness in the right

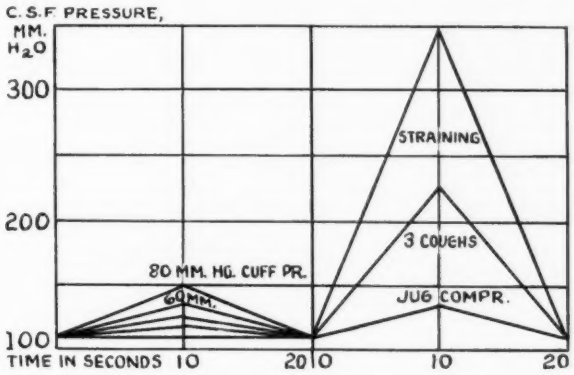

Chart 2.—Graph showing responses in the patient whose history is included in the text. The left half of the graph shows the very slight responses (from 108 to 150 mm. of water) in cerebrospinal fluid pressure on compression of the neck for ten seconds by cuff pressures of from 5 to 80 mm. As shown in the right half of the graph, however, the cerebrospinal fluid pressure rose promptly when the patient coughed or strained. The lower three lines at the left were obtained at cuff pressures of 5, 10, 20 and 40 mm. of mercury, respectively.

hand, forearm and arm and tingling in both arms. There was a partial Brown-Séquard paralysis, that is, motor weakness, accentuated deep reflexes, absent abdominal and cremasteric reflexes, plantar extension and diminished sensibility on the right side for touch, position and vibration. On the left, sensation to pain, heat and cold was diminished. The deep reflexes in the right upper extremity were reduced and power was greatly, though irregularly, diminished in the groups of muscles supplied by the right sixth, seventh and eighth cervical nerves. A roentgenogram was taken at the time of admission. A lumbar manometric test showed a practically complete subarachnoid block. With a constricting pressure of 80 mm. of mercury around the neck the cerebrospinal fluid pressure rose from

100 to 150 mm. of water. On the other hand, on coughing and straining the pressure rose rapidly to 220 and 350 mm., respectively.

The treatment consisted in the hyperextension of the neck by a plaster collar while in bed.

Nine days later there was considerable clinical improvement and the lumbar manometric test showed that the block had been partially relieved (chart 3). Two months later with continued improvement the lumbar manometric test was repeated with the results seen in chart 4. There was no evidence of block, and a roentgenogram taken at this time showed much less deformity.

In this patient the improvement would have been obvious by any method used. Manual jugular compression, however, would have been difficult because of the vertebral injury. In comparing the changes from time to time the fact that a known measured pressure had been used made the three tests much more comparable. Using this method

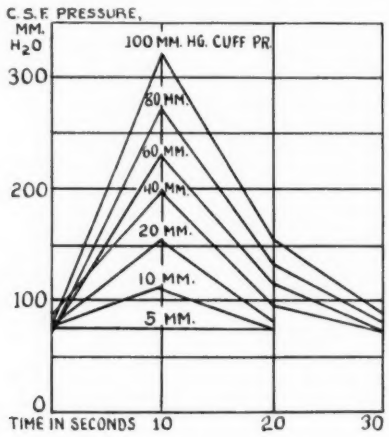

Chart 3.—Nine days after the neck was subjected to hyperextension, the responses are lower than normal and the rate of fall is prolonged. Nevertheless, there is marked improvement, as compared with results in chart 2.

of compression it has been interesting to follow at intervals cases of suspected tumors of the spinal cord and to see how nearly the results have corresponded in a given case when there have been no clinical signs of advance. This is not rendered less accurate by the fact that the findings have been recorded by different operators.

In some instances we recorded on a moving drum the pressure changes in the cuff about the neck and in the spinal canal, marking the time in seconds. The apparatus is still being perfected but many satisfactory tracings have been made. One such tracing is shown in chart 5. This offers numerous possibilities. A report on this work will be submitted at a later date.

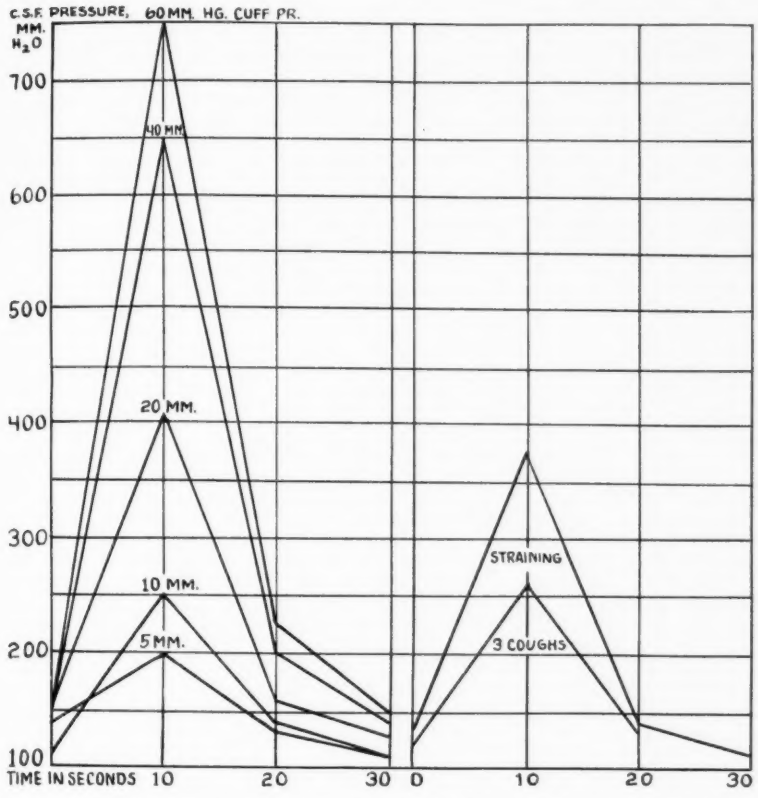

Chart 4.—Two months after treatment of the neck by hyperextension, the responses are very prompt and high and the pressure rapidly returns to its initial level. All evidence of block has disappeared. Compare with the results of earlier tests in charts 2 and 3.

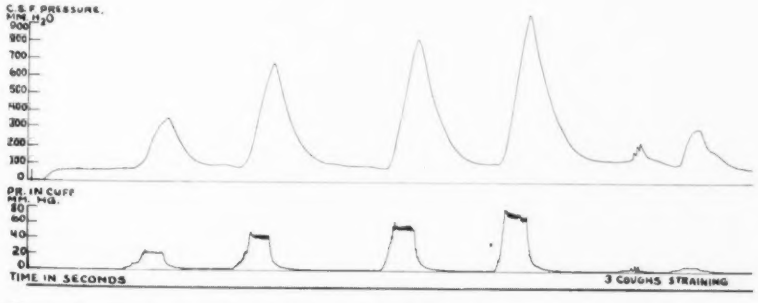

Chart 5.—Tracing made showing the changes in pressure after no evidence of subarachnoid block existed. The cerebrospinal fluid pressure is recorded above, the pressure in the cuff around the neck below, and the time is marked in seconds at the bottom.

COMMENT

The venous return from the brain takes place through the internal jugular and vertebral veins; that from the extracranial structures of the head, through the external jugular veins. The extracranial and intracranial circulations are connected through the various large emissary and diploic veins of the skull. The amount of blood returning from within the cranium by either of the channels outlined varies greatly under normal physiologic conditions.

Form Used for Recording the Results of the Lumbar Manometric Test

Name: Ward: Date:
Operator:
Clinical diagnosis:
Size of needle: Site of puncture:
Initial pressure: Color of fluid:
Oscillations: Cardiac:
Respiratory:

Cuff Pressure	Initial Pressure	After 10 Sec. Compr.	Pressure After Release			
			10 Sec.	20 Sec.	30 Sec.	40 Sec.
5 mm.						
10 mm.						
20 mm.						
40 mm.						
60 mm.						
80 mm.						
100 mm.						
3 coughs.						
Straining.						

Pressure after withdrawal of 7 cc. fluid:
Symptoms during test:
Cooperation during test:
Examination of fluid: total proteins
globulin
cells
Wassermann
colloidal gold
Conclusions:

With the method of accurately controlled jugular compression which has been outlined we have shown that it is possible to produce a graduated obstruction to the venous return. The great gap between momentary touch compression and deep jugular compression is eliminated. Partial blocks are more clearly proved.

The form we have been using for recording the findings during the manometric test is shown in the table.

SUMMARY

It is suggested that the graduated, measured jugular compression which can be obtained by applying a blood pressure cuff with its attached

sphygmomanometer to the neck provides a method for determining spinal subarachnoid block which has many advantages.

First, it gives a measured, graduated jugular compression which can be exactly duplicated in the same patient. Second, it makes possible a standard which can be used from patient to patient. Third, the results obtained by different operators are in much closer agreement and are therefore more dependable.

CEREBRAL CIRCULATION

XXXIII. THE EFFECT OF NERVE STIMULATION AND VARIOUS DRUGS ON THE VESSELS OF THE DURA MATER

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AND

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Although knowledge of the cerebral circulation has been increased of late years by direct microscopic study of the blood vessels of the pia mater, no similar observations on the vessels of the dura mater have been reported. Recently, Pickering [1] published important observations on the mechanism of headache produced by histamine. He presented strong evidence that the headache arises from an intracranial structure which is innervated by the trigeminal nerve, and that this structure is probably the dura. Reasoning from experimental data he suggested that the sensation of pain, in this type of headache at least, may be due to the stretching of a sensitive structure lying close to the meningeal arteries. Such stretching, he added, might conceivably arise from swelling of the perivascular tissues or from widening of the arteries. These observations are the outcome of carefully controlled experiments on human subjects. They open up a promising field of investigation. It seemed worth while, therefore, to undertake an investigation of the circulation of the dura mater, not only because the conception of intracranial dynamics cannot be considered complete without more information on this subject, but also because of the probable significance of the dura mater and its circulation in the etiology of headache.[2] Studies of the dural vessels were carried out, therefore, using much the same method as that developed in this laboratory for the study of the pial vessels.[3]

This work was aided by a grant from the Josiah Macy Jr. Foundation.

From the Neurological Unit, Boston City Hospital, and the Department of Neuropathology, Harvard University Medical School.

1. Pickering, G. W.: Observation on the Mechanism of Headache Produced by Histamine, Clin. Sc. **1**: 77, 1933.

2. Pool, J. L., and Nason, G. I.: The Cerebral Circulation: XXXV. The Comparative Effect of Ergotamine Tartrate on the Arteries in the Pia, Dura and Skin of Cats, Arch. Neurol. & Psychiat., to be published.

3. Forbes, H. S.: The Cerebral Circulation: I. Observation and Measurement of Pial Vessels, Arch. Neurol. & Psychiat. **19**:751 (May) 1928.

PROCEDURE

Healthy young cats were used in all cases but one, when a monkey (Macacus rhesus) was employed. The animals were anesthetized with an intraperitoneal injection of a 1 per cent solution of amytal (7 cc. per kilogram body weight).

The skull was then exposed and a trephine hole carefully drilled through to the dura mater. In the cat a comparatively large branch of the middle meningeal artery was usually uncovered by trephining in the region of the temporoparietal eminence. In the monkey a satisfactory exposure was made by an opening in the parietal bone tangential to the posterior border of the frontal bone and the superior border of the temporal. Bone wax[4] served to arrest bleeding. On completing the exposure the dura was gently irrigated with Ringer's solution warmed to body temperature. After screwing a cranial window into the trephine hole, further irrigation was resorted to by means of the hollow arms attached to the rim of the window. These were then tightly corked, leaving a thin layer of fluid between the glass and the dura, lest too great pressure of the dura against the window result in impairment of the circulation. Direct microscopic observations, measurements and photographs of the underlying dural vessels were then made.

During the preparatory procedure considerable technical difficulties were often encountered owing to the tendency of the freshly exposed dura to bleed, apparently due to rupture of pacchionian granulations or adherent veins. Hemorrhage of this nature was noticeably less frequent when young animals in obviously good condition were used. Hemorrhage could be arrested in some cases by immediate insertion of the window, with subsequent irrigation when indicated. It was rare, however, to obtain a field completely free from extravasated blood; but, unless excessive, the bleeding appeared in no way to affect the results. If excessive hemorrhage occurred, the experiment was discarded.

The blood pressure (measured in millimeters of mercury) was recorded by means of a cannula inserted into the femoral artery and attached to a mercury manometer. The cerebrospinal fluid pressure was measured by puncturing the occipito-atlantoid ligament and connecting the needle to a manometer filled with Ringer's solution. Nerve stimulation (faradic) was effected by means of a unipolar electrode which was attached to a Harvard inductorium supplied by one dry battery (the stimulation was usually for thirty seconds with a coil distance of from 10 to 12 cm.). The cephalic end of the ipsilateral vagus or cervical sympathetic nerve was stimulated, both nerves first being carefully dissected, tied and cut. Injections of drugs were made as specified, either intravenously or into the ipsilateral carotid artery, care being taken in the latter instance to avoid serious obstruction to arterial flow.

No experimental procedure was begun until a base-line of at least three (usually five or more) minutes had first been established. If no significant variations in blood pressure, spinal fluid pressure or size of the artery occurred during this interval, the experiment was begun. Four experiments were discarded in which the flow of blood through the dural vessels was visibly retarded either because of undue pressure against the window or because of the presence of excessive extravasated blood beneath it.

The changes in the diameter of the dural arteries, expressed in percentage, are shown in figure 4. In figure 7 a comparison is made under similar circum-

4. The bone wax which we used consists of beeswax, salicylic acid and oil of almonds.

stances between measured changes in the diameter of the arteries in the dura and those in the pia and in the skin. Photomicrographs of observed vessels before and after various procedures are appended.

COMMENT

In contradistinction to the pia mater, which with its blood vessels closely invests the underlying nerve tissue, the dura mater is a more independent structure which serves as a supporting and protecting medium for the brain and spinal cord; it contains also nutritive vessels which penetrate the bones of the skull.[5] Composed of mesenchymal tissue, it derives its chief blood supply from the internal maxillary artery via the middle meningeal artery. It is supplied also by branches from the vertebral, ophthalmic, ascending pharyngeal and occipital arteries. In the dura mater of man and of the cat, venous drainage is accomplished by a pair of veins, the venae comites, one of which lies on either side of the artery. According to Stöhr,[6] the nerve supply of the dura mater arises from three main sources: (1) the three branches of the trigeminal nerve (ophthalmic, maxillary and mandibular) giving rise to the tentorial, meningeal and recurrent spinosus nerves, respectively; (2) small branches from the ninth, tenth, eleventh and twelfth cranial nerves, and (3) sympathetic fibers, probably derived from the network surrounding the internal maxillary and middle meningeal arteries. Chorobski[7] described additional nerve fibers, which innervate the dura via the greater superficial petrosal branch of the seventh cranial nerve, and fibers to the middle meningeal artery by way of the auriculotemporal nerve.[8] Some nerve fibers have been demonstrated along the dural blood vessels, branching in the adventitia to be lost in the muscularis, while others, the nervii proprii, accompany the vessels and branch off into the connective tissue of the dura. Here they form an irregular network which, as Stöhr suggested, may have a sensory function responsive to changes in pressure or in the composition of the cerebrospinal fluid.

RESULTS

Stimulation of Nerves.—The results of the present experiments indicate that stimulation of the cephalic end of the cervical sympathetic

5. Piersol, G. A.: Human Anatomy, Philadelphia, J. B. Lippincott Company, 1908, vol. 2, p. 1198.

6. Stöhr, P.: Nerves of the Blood Vessels, Heart, Meninges, Digestive Tract and Urinary Bladder, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, p. 392.

7. Chorobski, J., and Penfield, W.: Cerebral Vasodilator Nerves and Their Pathway from the Medulla Oblongata, Arch. Neurol. & Psychiat. **28**:1273 (June) 1932.

8. Chorobski, J.: Personal communication to the authors.

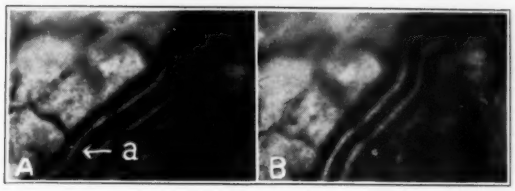

Fig. 1.—Photomicrographs (high power) of dural vessels taken with a Leica camera, Persenso film; obj. × 10; ocular × 10. *A* is the control; *B* was taken two minutes after sympathetic stimulation stopped (stimulation for forty-five seconds; coil distance, 10 cm.); *a* indicates the dural artery, on either side of which lie the venae comites. The decrease in diameter of this artery in *B* is very evident.

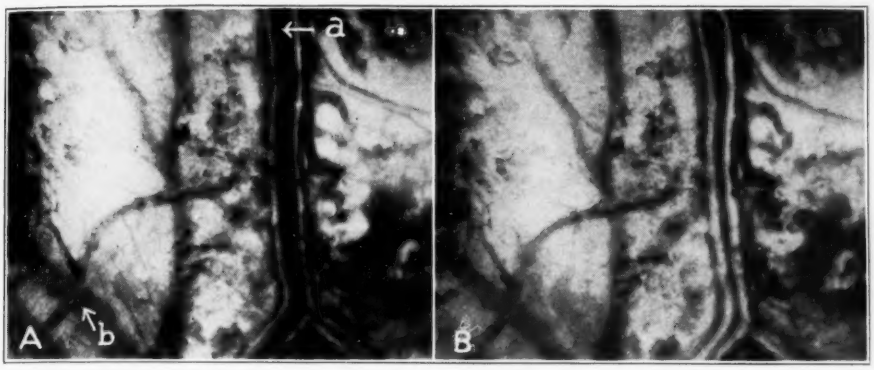

Fig. 2.—*A* is the control; *B* was taken during sympathetic stimulation, twenty seconds after stimulation started (coil distance, 12 cm.). The vessels in the background are pial vessels, seen through the dura; *a* is the dural artery and *b* is a pial artery which shows, in *B*, a barely perceptible constriction. The dural artery, on the other hand, shows a marked constriction. The slightly irregular constriction in *B* of figures 2, 3 and 5 is apparently caused by a slight degree of unavoidable trauma on insertion of the window. Low power; obj. × 3; ocular × 10.

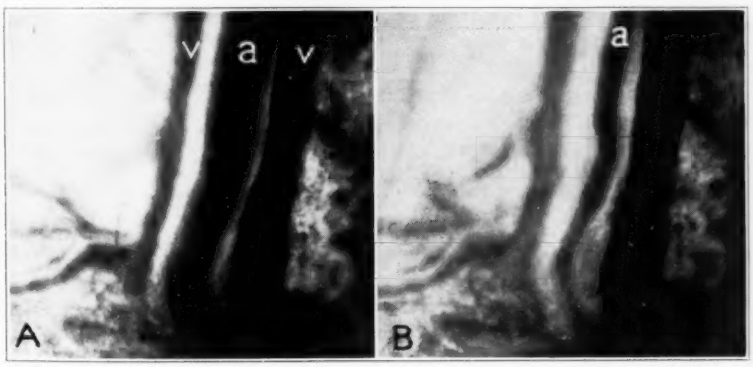

Fig. 3.—*A* is the control; *B* was taken twenty seconds after sympathetic stimulation stopped (thirty second stimulation; coil distance, 12 cm.); *a* indicates the dural artery; *v*, the venae comites. High power; obj. × 10; ocular × 10.

nerve causes a constriction of the ipsilateral dural arteries (fig. 1). In thirty-nine trials (on seventeen cats and one monkey) a significant change in the diameter occurred thirty-six times. In every instance this was a constriction, and the extent of change averaged 34 per cent. A visible retardation of both the venous and the arterial flow usually accompanied the stimulation; this was caused presumably by the vasoconstriction, for the blood pressure ordinarily did not fall.

Stimulation of the cephalic end of the vagus nerve (eleven trials on seven cats) was followed by arterial dilatation (averaging 15 per cent) five times, and by no change in diameter six times. Since vagal stimulation was generally accompanied by irregular changes in the rate and depth of respiration, it is impossible at this time to state whether the

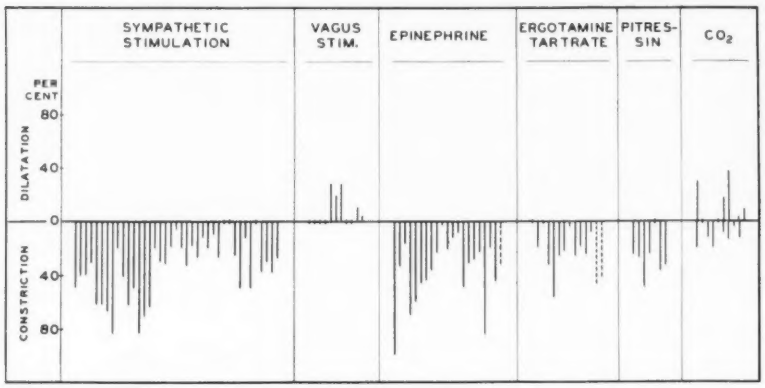

Fig. 4.—Each line represents the percentage change in diameter of the dural artery in a single experiment. Under epinephrine and ergotamine the broken lines show the effect of intracarotid injections. The results with ergotamine are discussed fully in another article.[2] They are included in this chart for comparison with the other data shown here.

dilating effect is due directly to vagal stimulation or to changes in blood chemistry (accumulation of carbon dioxide, etc.).

Drugs.—Epinephrine: Intravenous injection of epinephrine[9] (from 0.00054 to 0.0455 mg. per kilogram of body weight) each time resulted in a vasoconstriction. In twenty trials on fourteen cats the average arterial constriction amounted to a 29 per cent decrease in diameter (fig. 4). Intracarotid injection of epinephrine or its irrigation beneath the cranial window was followed also by rapid vasoconstriction. A retardation of flow in both arteries and veins was observed during the period of constriction after epinephrine, just as after stimulation of the sympathetic nerve.

9. Epinephrine tablets were dissolved in Ringer's solution.

In two experiments simultaneous observations of a pial and a dural artery were made, two microscopes and two windows being used, one on each side of the skull. The purpose of this procedure was to determine whether an intravenous injection of epinephrine was followed by the typical dilatation of the arteries in the pia (previously described [10]) coincident with constriction of the arteries in the dura. On both occasions this was found to be the case.

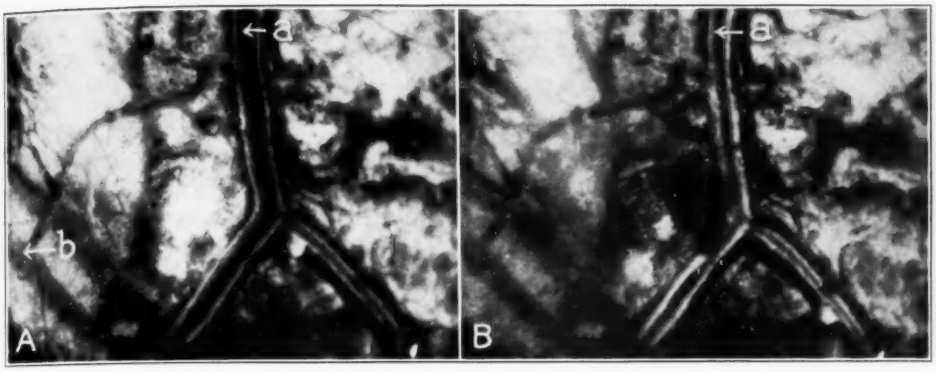

Fig. 5.—*A* is the control; *B* was taken seventy-five seconds after the intravenous injection of 0.6 cc. (1:100,000) of epinephrine (0.00286 mg. per kilogram); *a* is indicates the dural artery; *b*, a pial artery. These photomicrographs are from the same experiment as figure 2. The gradual increase in the hemorrhage is characteristic of the dural preparations. Low power; obj. × 3; ocular × 10.

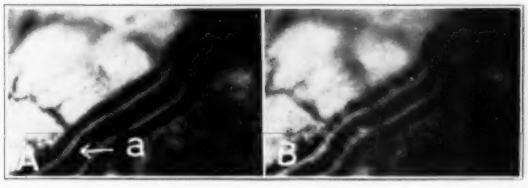

Fig. 6.— *A* is the control; *B* was taken fifty-five seconds after the intravenous injection of 0.6 cc. (1:100,000) of epinephrine (0.00286 mg. per kilogram); *a* is the dural artery. The beaded appearance of one of the veins clearly indicates a retardation of the venous flow. These photomicrographs are from the same experiment as figure 1. High power; obj. × 10; ocular × 10.

Pitressin: Pitressin [11] (0.5 cc. of a 1:10 solution) injected intravenously also resulted in vasoconstriction of the dural arteries. In seven

10. Forbes, H. S.; Finley, K. H., and Nason, G. I.: The Cerebral Circulation: XXIV. A. Action of Epinephrine on Pial Vessels; B. Action of Pituitary and Pitressin on Pial Vessels; C. Vasomotor Response in the Pia and in the Skin, Arch. Neurol. & Psychiat. **30:** 957 (Nov.) 1933.

11. Pitressin was dissolved in Ringer's solution 1:10, equaling 1 cc. of pitressin (20 pressor units) plus 9 cc. of Ringer's solution.

trials (on four cats) there was a significant change in diameter six times; the average decrease in diameter was 33 per cent.

The size of the artery apparently played no part in the degree of response to the procedures, small and large vessels reacting alike.[12] After constriction following any of the procedures just described, the artery usually resumed its original size after an interval of from three to ten minutes. The cerebrospinal fluid pressure, the blood pressure and the pulse and pupillary reactions exhibited the previously observed responses [13] to each procedure, and therefore are not specially mentioned in this report. The strength of the current and dosages of drugs were essentially the same as those used throughout this series of studies,[17]

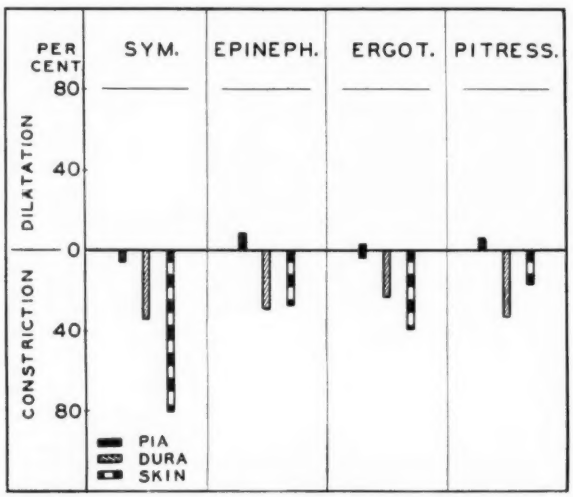

Fig. 7.—The contrast in reaction between the arteries of the pia and those of the dura and skin after sympathetic stimulation and the intravenous injection of epinephrine, ergotamine tartrate, and pitressin. The values for this figure were obtained from Forbes and his associates [12] and Pool and Nason.[2]

enabling a fair comparison to be made between the reaction of the arteries of the dura and the reaction of those in the pia and in the skin.

COMMENT

It is apparent (as shown in fig. 7) that on sympathetic stimulation the pial arteries are constricted less than the dural, and the dural less

12. This includes arteries measuring from 38 to 270 microns in diameter.

13. Forbes, H. S., and Wolff, H. G.: The Cerebral Circulation: III. The Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928. Wolff, H. G., and Lennox, W. G.: The Cerebral Circulation: XII. The Effect on Pial Vessels of Variations in the Oxygen and Carbon Dioxide Content of the Blood, ibid. **23**:1097 (June) 1930. Forbes, Finley and Nason.[10]

than the peripheral (skin) arteries. Moreover, epinephrine and pitressin, by intravenous injection, cause dilatation of the arteries in the pia, but constriction of those in the dura and the skin. Vagal stimulation results in dilatation of the dural arteries in less than half the cases; in the rest there is no change in the diameter. The pial arteries generally dilate.[13] Carbon dioxide, which consistently and strongly dilates the pial vessels, is extremely variable in its effect on those of the dura.

In general, the dural vessels react like those of the skin. The pial vasoconstrictor response is much weaker than the dural, so slight in fact that it may be completely overshadowed by the dilating force of a sharp rise in blood pressure. Thus, an intravenous injection of epinephrine is followed by arterial dilatation in the pia, but arterial constriction in the dura. The amount of change in the caliber of a vessel depends so much on the individual preparation (possible trauma, etc.), that a larger series of observations would alter, somewhat, the present figures.

SUMMARY

Various experimental procedures resulted in the following changes in caliber of the dural arteries:

1. Stimulation of the cervical sympathetic nerve—ipsilateral constriction (average decrease in diameter 34 per cent).
2. Stimulation of the vagus nerve—dilatation (average increase 15 per cent) or no change in diameter.
3. Injection of epinephrine—constriction (average 29 per cent).
4. Injection of pitressin—constriction (average 33 per cent).
5. Inhalation of carbon dioxide—inconstant results.

CONCLUSION

There is a close approximation between the degree of vasoconstriction in the dura and in the skin, both being considerably greater than that in the pia. Vasodilatation, on the other hand, is perhaps greater in the pia.

SPONGIOBLASTOMA POLARE OF THE PONS

CLINICOPATHOLOGIC STUDY OF ELEVEN CASES

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The term "spongioblastoma polare" is used to designate the group of slowly growing gliomas which are composed predominantly of unipolar and bipolar spongioblasts, and which occur with greatest frequency along or near the central axis of the brain from the medulla and pons posteriorly to the optic chiasm and optic nerves anteriorly. A series of these tumors from various locations was recently described by Bailey and Eisenhardt,[1] who discussed the terminology and the rather meager literature on the subject. The thirty-two cases reported by them from Cushing's clinic represent 1.57 per cent of the two thousand and twenty-three intracranial tumors in Cushing's collection [2] and 3.77 per cent of the eight hundred and sixty-two gliomas. Of the thirty-two tumors, five, or 15 per cent, were from the pons (0.25 per cent of the total number of tumors and 0.59 per cent of the gliomas). In Sachs' collection from this clinic are five hundred and forty-two intracranial tumors, of which two hundred and fifty (45 per cent) are gliomas.[3] There are sixteen examples of spongioblastoma polare (2.8 per cent of the total; 6.4 per cent of the gliomas), of which five arose in the pons (0.9 per cent of the total; 2 per cent of the gliomas).

Six additional cases are included in this study, three of which are from the laboratory of neuropathology of the Albert Merritt Billings Hospital and the Bobs Roberts Memorial Hospital of the University of Chicago Clinics and three from the Vanderbilt University Hospital and the department of pathology of the Vanderbilt University School of Medicine.[4]

Fellow in neurologic surgery, 1932-1933.

From the Departments of Neurological Surgery, Barnes Hospital and St. Louis Children's Hospital, and the neuropathologic laboratory of the Washington University Medical School, St. Louis.

1. Bailey, P., and Eisenhardt, L.: Spongioblastomas of the Brain, J. Comp. Neurol. **56**:391, 1932.

2. Cushing, H.: Intracranial Tumors, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

3. This number does not include twenty-eight "cysts," the histologic nature of which cannot be definitely verified.

4. Dr. Percival Bailey of Chicago and Dr. E. W. Goodpasture of Nashville gave permission to report these cases.

Few if any gliomas are composed entirely of one type of cell. On the contrary, many gliomas present distinctly different appearances in various areas, and the classification of such tumors depends, in the final analysis, on the predominating cell type. This fact was clearly pointed out by Bailey and Cushing [5] in their original classification, and has since been reiterated by Bailey.[6] It is particularly applicable to spongioblastoma polare, which is essentially a transitional tumor, lying histogenetically between the malignant primitive spongioblastoma multiforme and the benign mature astrocytoma. As might be expected, tumors of this type vary greatly in their cellular constitution. They fall naturally into three groups: a "primitive" type, a middle or "pure" type and a "mature" type.

At first glance the making of such a distinction might be thought to complicate further the already confusing complexity of existing classifications. However, it is hoped that by showing that these three apparently different types of tumors actually belong to one major group the picture will in reality be simplified.[7]

REPORT OF CASES

Of the eleven cases in this series, four presented tumors of the primitive type, three of the middle, or pure, type and four of the mature type. A brief résumé of each case is presented. The microscopic descriptions will be presented separately.

CASE 1.—*History.*—The patient, a white boy, aged 9 years, referred by Dr. Forster, Chicago, was admitted to the Bobs Roberts Memorial Hospital on Feb. 17, 1932. Three months before, he suddenly had a generalized convulsion with unconsciousness, which lasted for fifteen minutes. Following this he had high fever, sore throat and enlargement of the glands in the neck. He was prostrated; the head was retracted and the left eye turned inward. The infection subsided, but the boy continued to be restless and "queer," though he was up and about. Two months before admission his expression began to be vacant, his mouth often hung open, he frequently made vague, purposeless movements of the left hand and began to drag the left foot when he walked. When running he tended to fall to the left. He complained of headache and blurring of vision, and vomited several times. He was in bed for four weeks, and had one other generalized convulsion one week before admission.

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5. Bailey, P., and Cushing, H.: A Classification of Tumors of the Glioma Group on a Histogenetic Basis, Philadelphia, J. B. Lippincott Company, 1926.

6. Bailey, P.: (*a*) Cellular Types in Primary Tumors of the Brain, in Penfield, W.: The Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932; (*b*) Intracranial Tumors, Springfield, Ill., Charles C. Thomas, Publisher, 1933.

7. Dr. Pilcher has devoted a great deal of time and thought to the study of these cases, and his conception deserves careful consideration. I am as yet not entirely convinced that such a grouping will prove to be the most desirable. I have felt, in the past, that it might be wiser to group the borderline cases (his primitive and mature types) under the spongioblastoma multiforme group.—Ernest Sachs.

Examination.—The child was emaciated and lethargic, but cooperated when roused. The neck was slightly stiff. Both optic disks were choked. Ocular movements in the vertical plane were normal, but horizontal movements could not be performed. There was bilateral, partial ptosis, with evident involvement of the fifth, seventh, ninth, tenth, eleventh and twelfth cranial nerves on both sides,

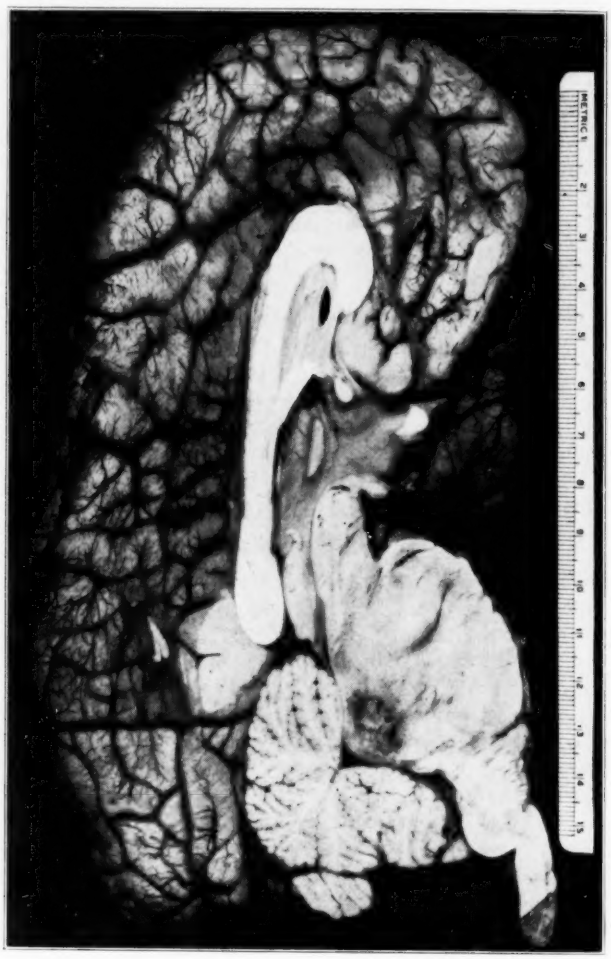

Fig. 1 (case 1).—Midsagittal section showing the aqueduct patent above but the fourth ventricle almost obliterated by the protruding mass of tumor. The tumor has infiltrated high into the brain-stem.

slightly more on the left than on the right. All the extremities were weak and hypotonic; the deep reflexes were diminished; there was no clonus or abnormal signs in the toes. The abdominal reflexes were absent on both sides. No nystagmus or definite ataxia was present. Roentgenograms showed no signs of pressure in the skull.

Lumbar puncture was performed on February 18 and 23. The pressure was from 50 to 70 and from 60 to 80 mm., respectively. The fluid was normal in every respect.

Course.—The child grew steadily worse, and died on February 27. The clinical diagnosis was encephalitis.

Necropsy.—A large nodular tumor involved the entire pons and the cephalic end of the medulla (fig. 1). It extended into the upper brain stem to the level of the red nucleus, but not into the cerebral peduncles. The third nerves were

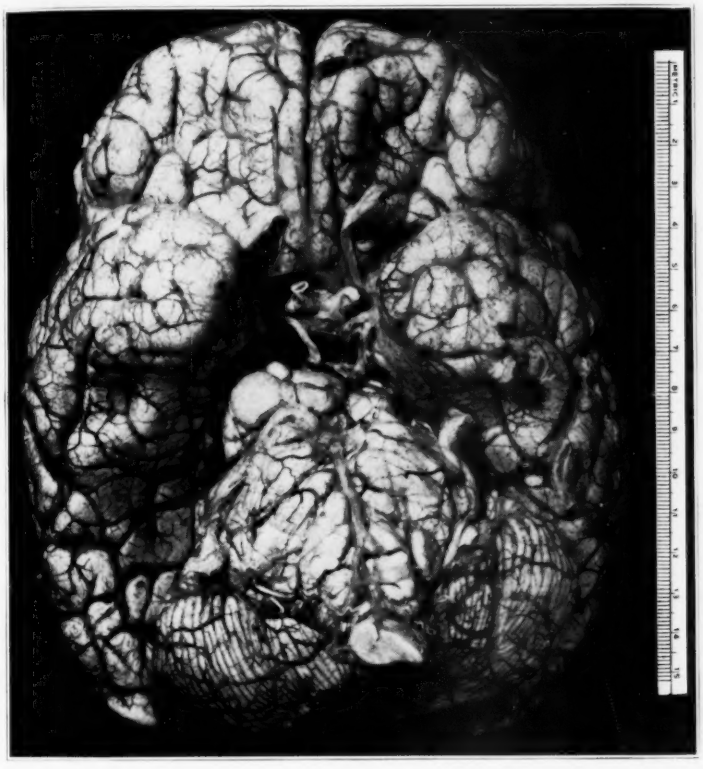

Fig. 2 (case 2).—Note the nodular structure of the tumor, with distortion of the normal relationships. The cranial nerves emerge from the tumor itself, and it is difficult to distinguish one from the other (fig. 6*A*).

free externally, and the corpora quadrigemina were not involved or compressed. The tumor could be seen between fiber bundles in both cerebellar peduncles. In the floor of the fourth ventricle a large degenerated cystic area extended to the right more than to the left. All the nerves arising from the brain stem seemed to emerge from the substance of the tumor. The aqueduct was patent and not greatly dilated, and there was only slight dilatation of the third and lateral ventricles. Microscopically the tumor was of the primitive type of spongioblastoma polare (fig. 10).

CASE 2.—*History.*—A white boy, aged 4 years, referred by Dr. Joseph Brennemann, was admitted to the University of Chicago Clinics on Dec. 2, 1931, with

a history of the sudden onset, five weeks previously, of vomiting, headache, "nodding" (inability to hold the head up) and deviation of his eyes to the left. Careful questioning of the parents elicited no history of previous illness except that the child seemed irritable and vomited twice in the five preceding months. The symptoms progressed rapidly; he tended to fall to the left and to drag the left foot. The voice became nasal and speech difficult to understand.

Examination.—On admission, the child lay quietly and cooperated well. The voice was distinctly nasal. McEwen's sign was present. The optic disks showed no measurable swelling, but the margins were hazy, and the retinal veins were distended. There were limitation in the upward movement of both eyes and bilateral weakness of the sixth nerve, but no ptosis. The seventh, ninth, tenth and twelfth cranial nerves were involved on the left side, and there was marked left hemiparesis with hyperactive reflexes and ankle clonus (the latter was bilateral). A slow nystagmus was present on looking to either side or upward. Roentgenograms showed no abnormality. The clinical diagnosis was pontile tumor.

Operation and Course.—A suboccipital exploration by Dr. Paul Bucy on Dec. 7, 1931, disclosed an inoperable tumor of the pons and medulla. The symptoms steadily progressed, and the child died on December 31.

Necropsy.—A huge, irregularly nodular tumor involved the entire pons and most of the medulla (fig. 2). It extended high into the midbrain on the right side, compressing the cerebral peduncle into a thin strip of fibers. The third nerves and the corpora quadrigemina were greatly flattened, and the remainder of the cranial nerves on both sides were involved in the tumor. There was no gross degeneration. The fourth ventricle and aqueduct were completely obliterated, and there was marked internal hydrocephalus. The tumor was of the primitive type of spongioblastoma polare (figs. 6 *A* and 9 *A*).

Case 3.—*History.*—A white girl, aged 3 years, referred by Dr. E. Moody, Joplin, Mo., was admitted to the St. Louis Children's Hospital in a moribund state. Three weeks before she began to stagger and, shortly thereafter, to drag the left foot. The physician observed ataxia of the left hand and a positive Babinski sign on the left. The spinal fluid was normal. She became rapidly worse, vomited frequently and grew more and more lethargic.

Examination.—On admission, the child was moribund and cyanotic and had Cheyne-Stokes respiration. The retinal veins were full, but there was no choking. All reflexes were absent. She died before further examination could be performed.

Necropsy.—There was a firm, white, nodular tumor of the same type as described in the preceding cases. The entire pons was involved, but only on the right side were the normal structures completely replaced by the tumor. The tumor did not extend into the midbrain or involve the medulla. The fourth ventricle and aqueduct were open, and there was no dilatation of the third or lateral ventricles. Microscopically it was of the primitive type of spongioblastoma polare.

Case 4.—*History.*—A married white woman, aged 29, referred by Dr. A. B. Jones, St. Louis, was admitted to the Barnes Hospital on Oct. 12, 1926. On July 20 double vision suddenly developed and the right eye was turned inward. A month later, with no new symptoms, a spinal puncture was done in another city. The spinal fluid was normal. Two days later there developed violent headache and almost continuous vomiting; subsequently the left arm and leg became numb. Two weeks before admission the patient first had difficulty in swallowing, and a week later she began to be dizzy and to have occasional twitching of the left facial muscles.

Examination.—The patient was cheerful and alert. The eyegrounds were normal. The fifth, sixth and seventh cranial nerves on the right were involved, and there was occasional fibrillary twitching of the left facial muscles. Marked hemiparesis and hemihypesthesia were present on the left, and nystagmus was seen on both upward and lateral gaze. The diagnosis made was tumor of the pons or cerebellum.

Operation.—On Nov. 3, 1926, Dr. Sachs operated in the hope that the lesion might be cerebellar, but the tumor was not disclosed, and early death occurred.

Necropsy.—Examination was limited to a study of the brain through the operative wound. This revealed a tumor of the pons, with a large nodule on the right side and a smaller one on the left. It did not apparently extend upward into the midbrain or downward into the medulla. Microscopically, it was the primitive type of spongioblastoma polare.

CASE 5.—*History.*—A white boy, aged 5 years, was admitted to the St. Louis Children's Hospital on Feb. 3, 1926. Fourteen months before, the parents first noticed that he moved his head rather than his eyes when changing the direction of gaze, but the details of this are not clear. It was not until five months before admission that he began to show an unsteady gait, with a tendency to fall forward, awkwardness in the use of the hands, and frequent vomiting and headaches. During the two weeks prior to admission all symptoms grew steadily worse. However, exact information as to the movements of the eyes is lacking.

Examination.—The child was quite ill and cooperated poorly. He made peculiar purposeless movements with his hands. The optic disks were choked. Conjugate deviation of the eyes upward was normal, but there was bilateral weakness of the external rectus muscles. There was no other involvement of the cranial nerves, but all four extremities were weak and the reflexes exaggerated. The ankle clonus and dorsal responses in the toes were bilateral. Both arms were ataxic, but there was no nystagmus. Roentgenograms showed marked separation of the sutures. The clinical diagnosis was cerebellar tumor.

Operation and Course.—A suboccipital exploration on Feb. 10, 1926, by Dr. Sachs failed to show the lesion. A ventricular puncture during the operation indicated marked dilatation. The symptoms progressed, and the child died on February 18.

Necropsy.—There was a large firm tumor in the floor of the upper portion of the fourth ventricle, apparently arising from the pars dorsalis of the pons. Unlike the other tumors in this series, this tumor was for the most part well demarcated, and seemed in some places to have a definite capsule. It definitely invaded the already compressed surrounding tissue only along the dorsal surface of the pons. Here it extended to a moderate depth, probably just deep enough to involve the nuclei of the sixth nerves. The great mass of the tumor completely obstructed the fourth ventricle. Both hemispheres of the cerebellum were markedly compressed. Unfortunately, the cerebral hemispheres were not preserved, and there is no record of the presence of the hydrocephalus which was demonstrated at operation. Microscopically the tumor was of the pure type of spongioblastoma polare (fig. 8*A*).

CASE 6.—*History.*—A Negro, aged 19, was admitted to the Vanderbilt University Hospital on Nov. 5, 1931, with a history of ringing in the left ear for ten months, which was followed by slowly progressive deafness on that side. After three months he began to be dizzy and to have attacks of severe headache, and there developed progressive weakness of the right leg and arm and of the left side of the face, including the upper portion. Soon the patient began to vomit,

and the left side of the face became numb. For at least six months the eyes had been turned inward and he had had marked diplopia.

Examination.—The patient was apathetic and dull, but rational. The eyegrounds were normal. There were bilateral paralysis of the sixth nerve and involvement of the left fifth, seventh and eighth nerves, but the tongue protruded to the right. The entire right side was weak, and sensation was diminished. The reflexes were more active on the right. No clonus or abnormal signs in the toes were present. There was no ataxia or nystagmus. The clinical diagnosis was tumor of the left portion of the eighth nerve.

Operation and Course.—Suboccipital exploration by Dr. T. D. McKinney on November 11 revealed an inoperable tumor arising from the pons in the left cerebellopontile angle. The patient failed to rally after the operation and died that night.

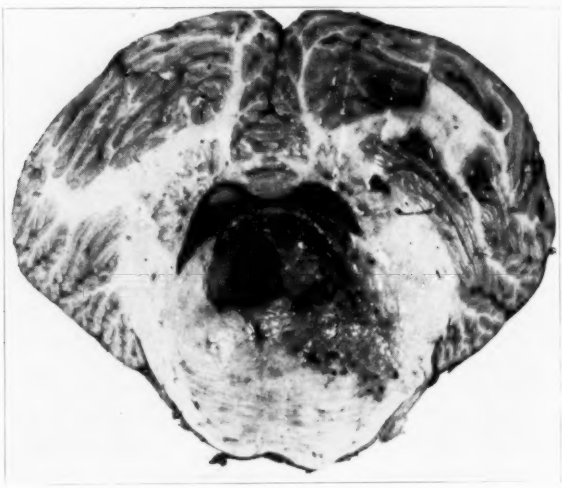

Fig. 3 (case 6).—Coronal sections showing the huge cyst and the invasion of the left brachium pontis.

Necropsy.—There was a large, irregular tumor in the substance of the pons (fig. 3). It did not extend into the midbrain. The third nerve was not involved. The upper left side of the pons was almost entirely destroyed by the tumor, and a large cyst extended beyond the midline. The fourth ventricle was elongated transversely; nevertheless, it was definitely dilated, and there was marked dilatation of the aqueduct and third ventricle. The lateral ventricles were moderately dilated. The tumor was the pure type of spongioblastoma polare (fig. 7 *B*).

Case 7.—*History.*—A German woman, aged 35, married, was admitted to the University of Chicago Clinics on Sept. 23, 1931, referred by Dr. E. Grimm, Chicago. Seven months previously her left ear drum ruptured spontaneously, and the ear had been discharging since. Two months before admission she became unsteady on her feet and began to have severe headaches. A month later she began to vomit frequently, and an operation was performed for "intestinal obstruction." She continued to vomit, was irrational and was incontinent at times. The neck became stiff, and movement of the head was painful. On the day before admission she had difficulty in breathing, perspired freely and the pulse was rapid.

Examination.—On admission, the patient was somewhat confused, pale and slightly cyanotic. The neck was stiff; there was some tenderness in the left suboccipital region; a purulent discharge was seen in the left auditory canal and a small perforation of the drum. The left pupil was smaller than the right and did not react to light. There was a recent fresh corneal ulcer on the left, with advanced choking of both optic disks. Conjugate deviation to the left was greatly impaired, and there was moderate ptosis of both eyelids. There was marked involvement of the left fifth, seventh, eighth and ninth cranial nerves. Both sensory and motor function were impaired in the right arm and leg, and there seemed

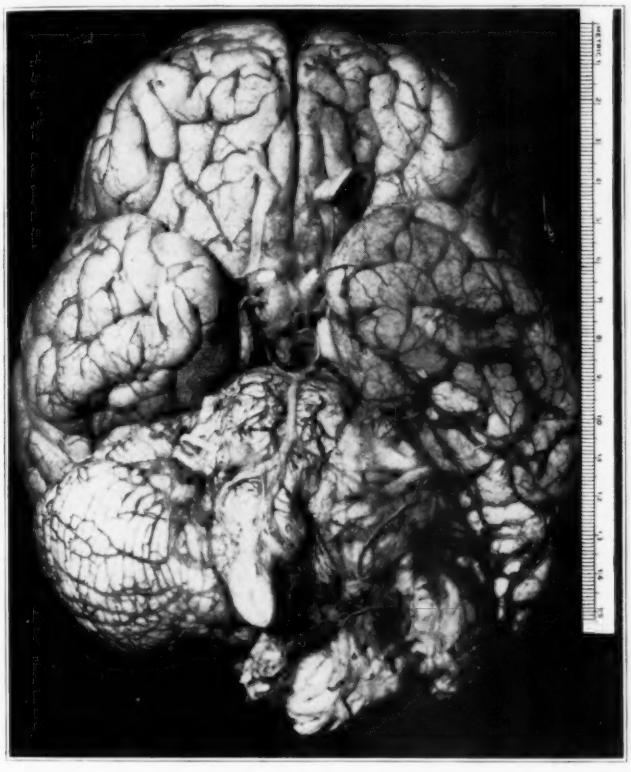

Fig. 4 (case 7).—The huge tumor extends far to the left; the distortion of the seventh and eighth nerves mentioned in the text is clearly seen.

to be some weakness of the left extremities as well. All deep reflexes were absent, and the extremities were hypotonic. There was marked, slow nystagmus in all directions; the left arm was coarsely ataxic. Roentgenograms revealed no abnormalities. The clinical diagnosis was probable abscess in the left portion of the cerebellum.

Operation and Course.—A suboccipital exploration performed on September 24 by Dr. Bucy gave negative results. A decompression was done. The patient improved for a time and was discharged on October 21. When seen on November 16 the neurologic signs were the same, but the general condition was good. Vom-

iting occurred about once a day. However, on December 14, she returned to the hospital with increasing stupor and mental confusion and an advance of all neurologic signs. Roentgenograms showed dilatation of the left internal acoustic meatus, and it was thought that the patient probably had an acoustic tumor.

Dr. Bailey reexplored the cerebellum and discovered a firm tumor deep in the left cerebellar hemisphere. A large portion was removed. After the operation there was respiratory difficulty, and the patient died on the following day.

Necropsy.—A huge tumor of the left side of the pons extended well into the cerebral peduncle and far out under and into the left cerebellar hemisphere (fig. 4). The petrous bone was eroded and the internal acoustic meatus enlarged. The seventh and eighth nerves, which arose from the substance of the tumor, showed a definite collar formation at their entrance into the meatus. No cystic areas were present. There was no hydrocephalus, and the convolutions were not flattened. The tumor was of the pure type of spongioblastoma polare (figs. 7 *A* and 8 *B*).

Case 8.—*History.*—A white girl, aged 8 years, referred by Dr. G. B. Fletcher, Hot Springs, Ark., and Dr. I. G. Mitchell, Eldorado, Ark., was admitted to the St. Louis Children's Hospital on Nov. 27, 1931. Four months before admission it was first noticed that the head was tilted to the right; a month later the right eye turned inward, and the child began to have headaches. Soon she had vertigo and began to drag the left leg. For a month she had been deaf in the right ear, and had been vomiting frequently.

Examination.—The right pupil was larger than the left. The retinal veins were full, but there was no measurable swelling of the disks. Conjugate movement of the eyes to the right was impossible, and there was a right internal squint. The fifth, seventh, eighth, ninth, tenth, eleventh and twelfth cranial nerves were involved on the right and there were hemiparesis and hemihypesthesia on the left. Roentgenograms revealed no abnormalities. The clinical diagnosis was tumor of the pons.

Operation and Course.—Suboccipital exploration performed on December 1, by Dr. Sachs, disclosed an inoperable tumor of the pons. The patient died soon after the operation.

Necropsy.—A large tumor of the right half of the pons extended upward to the corpora quadrigemina. There were no cystic areas. The aqueduct and fourth ventricle were open and not dilated, though somewhat distorted, and there was no hydrocephalus. The tumor was of the mature type of spongioblastoma polare.

Case 9.—*History.*—A white girl, aged 4 years, admitted to the St. Louis Children's Hospital on March 17, 1932, had a fall three months before without apparent injury; since that time, however, she had vomited every three or four days. Three weeks after the injury she began to stagger, and complained of being dizzy. Speech became slurring and indistinct. A spinal puncture was done by her physician, who reported that the fluid was under increased pressure, but otherwise normal.

Examination.—The child was well oriented, but inattentive; the mouth stayed open; the head was tilted to the left. Enunciation was indistinct, and the voice was nasal. The eyegrounds and extra-ocular muscles were normal except for a slow nystagmus in all directions. There was involvement of the fifth and ninth nerves on both sides and of the seventh on the right. No definite weakness of the extremities was detected, but bilateral Babinski and Oppenheim signs were present. The gait was ataxic, but there was no ataxia of the arms. Roentgenograms showed

marked convolutional atrophy. The clinical diagnosis was subdural hematoma, or tumor, probably in the posterior fossa. Ventriculography was advised, but was refused by the parents.

Course.—The patient was taken home, where she grew rapidly worse. On June 3, she was brought back to the hospital with spastic hemiplegia on the right and bilaterally choked disks. She was semistuporous and did not speak, but she understood simple commands.

Ventriculograms, made on June 4 by Dr. R. M. Klemme, showed marked internal hydrocephalus; cerebellar exploration failed to disclose the tumor. The child reacted satisfactorily, but the symptoms grew steadily worse. Exploration of the superior surface of the cerebellum by a transtentorial approach on June 25 by Dr. Sachs revealed a tumor deep in the vermis and extending into the pons. Only a small portion could be removed, and the child died of sudden respiratory failure on the afternoon of the day of operation.

Necropsy.—A large lobulated tumor of the pons extended posteriorly to flatten the vermis, completely occluding the aqueduct. Externally, the tumor was much larger on the left. A large nodule extended up under the base almost to the optic chiasm, and inferiorly the upper left portion of the medulla was compressed and distorted by another mass of the growth. However, on section it was seen that the substance of the pons on the right side was almost completely replaced by the tumor, in which were several small cystic areas. There was marked internal hydrocephalus. The tumor was of the mature type of spongioblastoma polare.

CASE 10.—*History.*—A white girl, aged 4 years, referred by Dr. Ed Fisher, Lebanon, Tenn., was admitted to the Vanderbilt University Hospital on Oct. 1, 1929. Two months before, while she was recovering from "colitis," it was observed that the right eye began to turn in. This condition grew worse, and shortly afterward she began to drag the left foot. After two weeks she had become less active and appeared drowsy. By the end of the first month she could not move the left arm or leg, and she had severe headaches and frequent attacks of vomiting. Soon speech became thick and indistinct, and the tongue seemed swollen.

Examination.—On admission the child was drowsy, but irritable when aroused, and the examination was not satisfactory. The eyegrounds were normal; vision was unimpaired. The external rectus muscle and facial muscles on the right and the entire left half of the body were almost completely paralyzed. Ankle and patellar clonus were elicited on both sides, and a Babinski sign was present on the left. Speech was slurring, and the enunciation was poor. Roentgenograms revealed no abnormalities. The spinal fluid was not under increased pressure, nor was it otherwise abnormal.

Course.—The child grew rapidly worse. Weakness of the left sixth nerve appeared, and there was occasional twitching of the left arm. She vomited repeatedly. Death occurred on October 7. The clinical diagnosis was encephalitis.

Necropsy.—There was a firm, lobulated tumor of the pons. It masked the entire ventral surface of the pons but extended much lower on the right, compressing the upper portion of the medulla. On section, it was seen to occupy the entire right side of the pons, whereas on the left the tumor extended between bands of nerve tissue. It extended upward to the incisura, but not into the midbrain. There was no gross cyst formation or degeneration. No hydrocephalus was present. The tumor was of the mature type of spongioblastoma polare (fig. 11).

CASE 11.—*History.*—A white girl, aged 10 years, died as she was brought into the emergency room of the Vanderbilt University Hospital on April 27, 1926. Four

months before she began to hold her head to the right and to be irritable and careless. Two months later she became unsteady on her feet, used the right hand poorly, and speech became slurred and difficult to understand. According to the family physician, spastic paralysis of the right arm and leg developed rapidly, the head was turned constantly to the right and the external rectus muscle on the left was paralyzed. There was no visual disturbance or headache. No mention of vomiting is made in the brief record.

Necropsy.—There was a firm, irregular tumor of the pons, which was larger on the left side (fig. 5). It extended from the medulla through the pons and into the basis pedunculi on the left side. Numerous small cystic areas were present. The aqueduct was patent, and the ventricles were not dilated. The tumor was of the mature type of spongioblastoma polare.

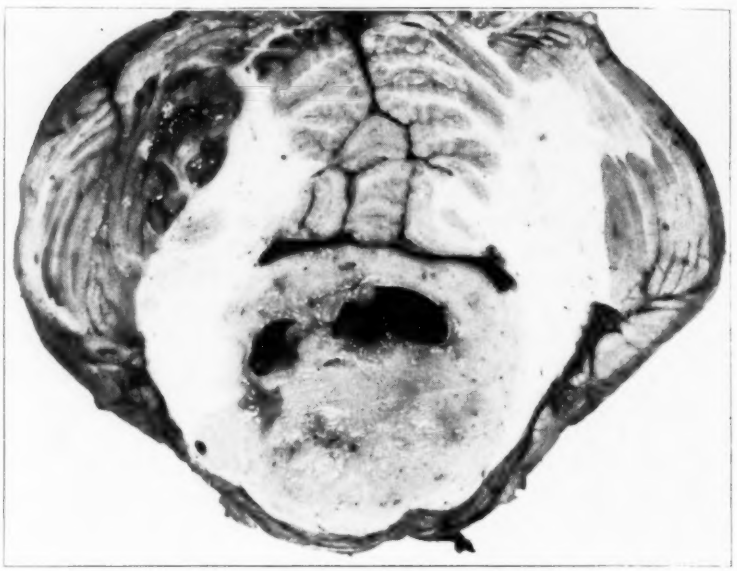

Fig. 5 (case 11).—Coronal sections showing the entire pons diffusely involved. The cysts are clearly outlined, with little or no surrounding degeneration.

MICROSCOPIC OBSERVATIONS

The outstanding cytologic feature of these tumors is their transitional nature. The structure and histologic appearance of the tumors varies greatly; even in one tumor sections from different portions frequently present very different pictures. The tumors are here divided into three groups, solely to emphasize the wide variations that may exist, and to point out that many gliomas which do not conform to the classic picture of spongioblastoma polare nevertheless belong in this group. All the tumors included here present microscopic evidence of slow growth; all contain large numbers of polarized spongioblasts and all tend to invade centrifugally between fiber bundles, so that often the

size of the pons may be tremendously increased, though there is only a small area of solid tumor (figs. 1, 2 and 6). Further, as will be seen, the clinical behavior is much the same.

At some places on the periphery of the tumors there is a marked glial reaction, which sometimes can be distinguished with difficulty from actual neoplastic tissue.

Pure Type.—This tumor is the middle type, the true spongioblastoma unipolare (or "unipolare et bipolare") of Bailey and Cushing,[5] the "spongioblastoma polare" of Penfield,[8] the "oligodendrocytome à cellules fusiformes" of Roussy and Oberling,[9] the "Neurinoma zentrale" of

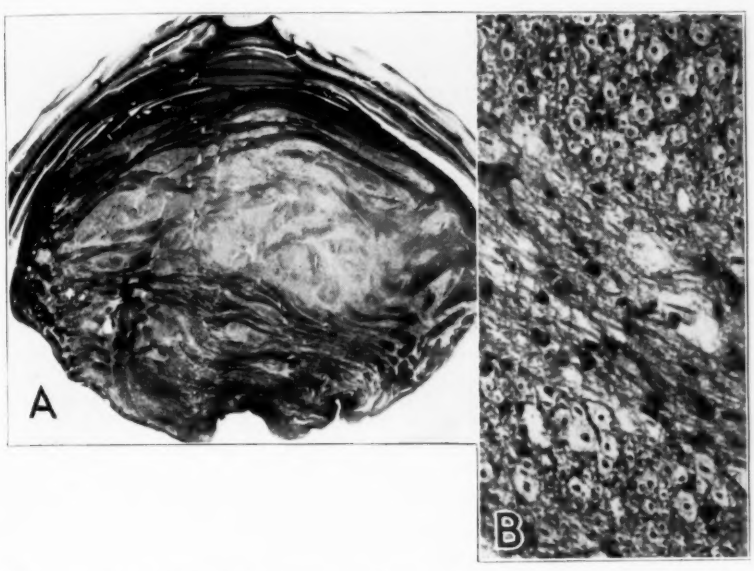

Fig. 6.—Extension of the tumor between the fiber bundles. *A* (case 2), a coronal section of the pons, shows large bundles of fibers which remain in the center of the area of tumefaction, and the tumor which extends between the flattened fiber tracts below. The fourth ventricle is obliterated. Pal-Weigert stain; actual size. *B* (case 11), streams of tumor cells extend between the nerve bundles, which are cut transversely. Phosphotungstic acid and hematoxylin stain.

Josephy,[10] and the "spongioblastoma" of Bailey and Eisenhardt.[1] Three examples occur in this series. They are composed of streams of parallel,

8. Penfield, W.: Principles of the Pathology of Neuro-Surgery, in Nelson's Loose-Leaf Living Surgery, New York, Thomas Nelson & Sons, 1927, vol. 2, p. 347 *A*.

9. Roussy, G., and Oberling, C.: Les tumeurs des centres nerveux et des nerfs périphériques, Atlas du cancer, Paris, Félix Alcan, 1931, pts. 9 and 10.

10. Josephy, H.: Ein Fall von Parabulbie und solitärem zentralem Neurinom, Ztschr. f. d. ges. Neurol. u. Psychiat. **93**:62, 1924.

elongated cells with long, wavy processes (fig. 7). The streams of cells swirl in all directions. Their resemblance at times to the acoustic fibroblastomas has often been noted.[11] In other areas they have the appearance of elastic tissue (such an area in a tumor of the mature type is shown in figure 11 *B*). However, no connective tissue elements can be demonstrated in them by specific staining methods. Moreover,

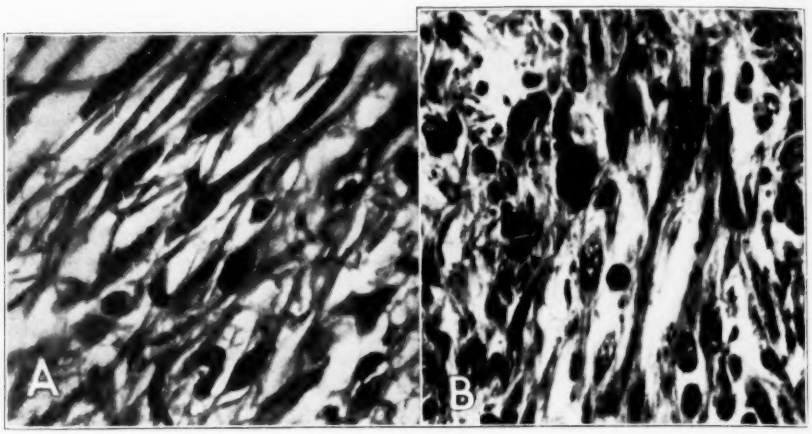

Fig. 7.—Pure type of spongioblastoma polare. The parallel polarized cells, with heavy protoplasmic extensions, are well shown in both tumors: *A*, section from case 7; hematoxylin and eosin; *B*, section from case 6; phosphotungstic acid and hematoxylin.

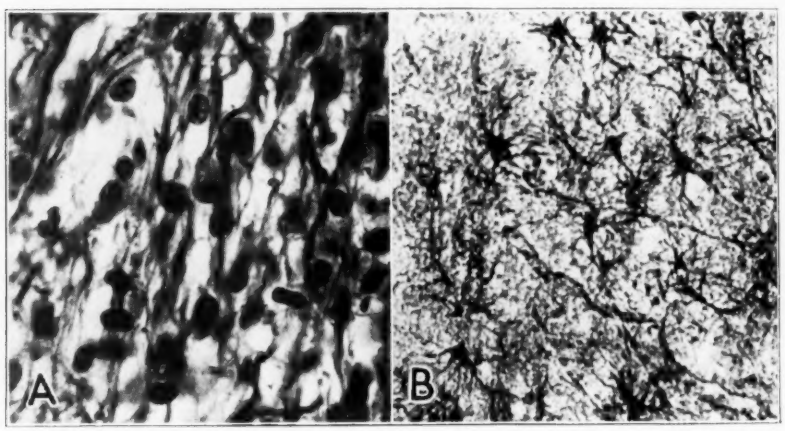

Fig. 8.—Pure type of spongioblastoma polare. *A* (case 5), note the long, parallel processes; silver carbonate. *B* (case 7) shows gliosis at the margin of the tumor. Gold chloride-mercuric chloride (modification of Globus' method).

11. Bailey and Eisenhardt.[1] Josephy.[10]

silver impregnation (fig. 8 *A*) shows the cells to be identical with the spongioblasts in the developing nervous system (de Castro [12]).

The nuclei are oval or elliptic (when cut in the plane of their long axes) and stain well with hematoxylin. The cytoplasm is rather scanty, except for its extension into the long, heavy processes which arise from one or both poles of the cells. Even in this pure type of tumor numerous astrocytes and transitional cells can be seen. No mitotic figures are present, and the tumors are surprisingly avascular. There is practically no cellular degeneration in most sections. Even in the most cellular parts of the tumors nerve fibers can be seen in large numbers and an occasional ganglion cell remains. No calcification is encountered.

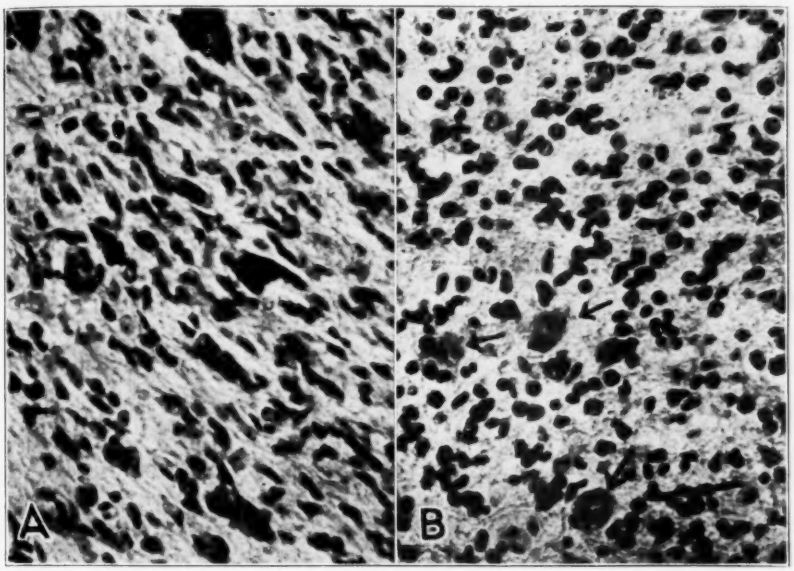

Fig. 9.—Primitive type of spongioblastoma polare. The tumors are cellular, and the nuclei vary greatly in size and shape. *A* (case 2) shows numerous giant cells, some of which are completely hyalinized, but higher magnification reveals no mitoses. Hematoxylin and eosin. *B* shows numerous ganglion cells which have been "trapped" in the center of the tumor, marked by arrows; some are disintegrating. Hematoxylin and eosin.

At the peripheries of the tumors there is frequently a marked reaction of the fibrillary neuroglia (fig. 8 *B*).

Primitive Type.—These tumors at first glance closely resemble the malignant spongioblastoma multiforme. They are more cellular than the foregoing pure type. Their cells vary greatly in size, shape and

12. de Castro, F.: Algunas observaciones sobre la histogenesis de la neuroglia en el bulbo olfactivo, Trab. du lab. de invest. biol. Univ. de Madrid **18**:83, 1920; also in Arch. de neurobiol. **1**:49, 1920.

staining qualities. The nuclei are often of bizarre shapes and, in two of the four examples presented, true tumor giant cells are seen (fig. 9). However, on closer examination it is seen that these tumors are essentially benign. Mitotic figures are not seen, and the intervascular degeneration with palisading of nuclei, which is characteristic of spongioblastoma multiforme, does not occur. Furthermore, they lack the vascularity of the more malignant tumor. Careful examination shows that nearly all the tumor cells are unipolar or bipolar spongioblasts, though many are distorted and irregular (fig. 10). For the most part there is no particular arrangement of the cells, but in some areas streams of more mature cells resemble the pure type. A few

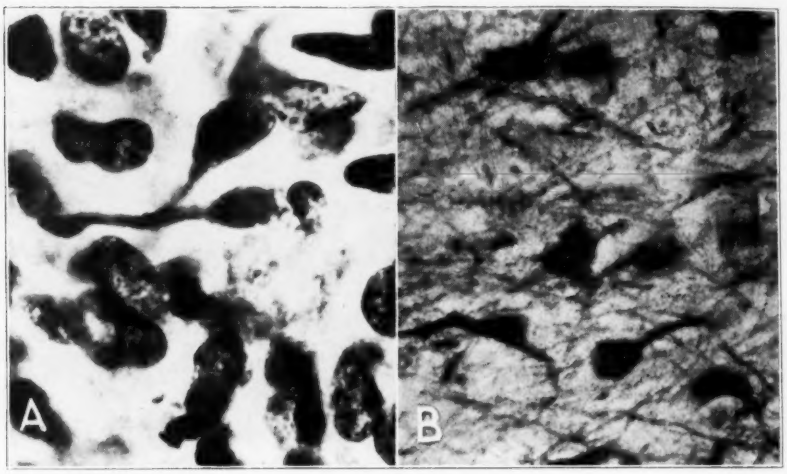

Fig. 10.—Primitive type of spongioblastoma polare. *A* (case 1) shows a detail of unipolar spongioblasts. Tannic acid-silver nitrate (Hortega IV). B shows bizarre shapes in an area in which the cells are dissociated by edema. Gold chloride-mercuric chloride (modification of Globus' method).

astrocytes are seen; many of the unipolar spongioblasts have short, protoplasmic projections from their unpolarized ends (fig. 10 *B*).

These tumors, then, form the transitional stage between the malignant spongioblastoma multiforme and the benign spongioblastoma polare. The four tumors in this series are essentially benign and should be classified with the latter group. One (case 4) was formerly classified as spongioblastoma multiforme and was reported as such by Dr. Sachs.[13] It is possible that similar tumors have been differently classified in other clinics.[14] This may well account for the discrepancy in percentages

13. Sachs, E.: The Diagnosis and Treatment of Brain Tumors, St. Louis, C. V. Mosby Company, 1931, p. 274, case 32.

14. Buckley, R. C.: Pontile Gliomas, Arch. Path. **9**:779 (April) 1930.

already noted between the collections of Dr. Cushing and Dr. Sachs. It should not be forgotten, however, that some portions of malignant tumors in this location may contain streams of spongioblasts, and are easily mistaken for the type of tumor herein described.

Mature Type.—About the classification of the four tumors in this group there might arise a justifiable difference of opinion. All contain large areas of astrocytes. Indeed, some entire sections present the characteristic picture of an astrocytoma (fig. 11 *A*). However, other equally large areas of all these tumors are composed predominantly

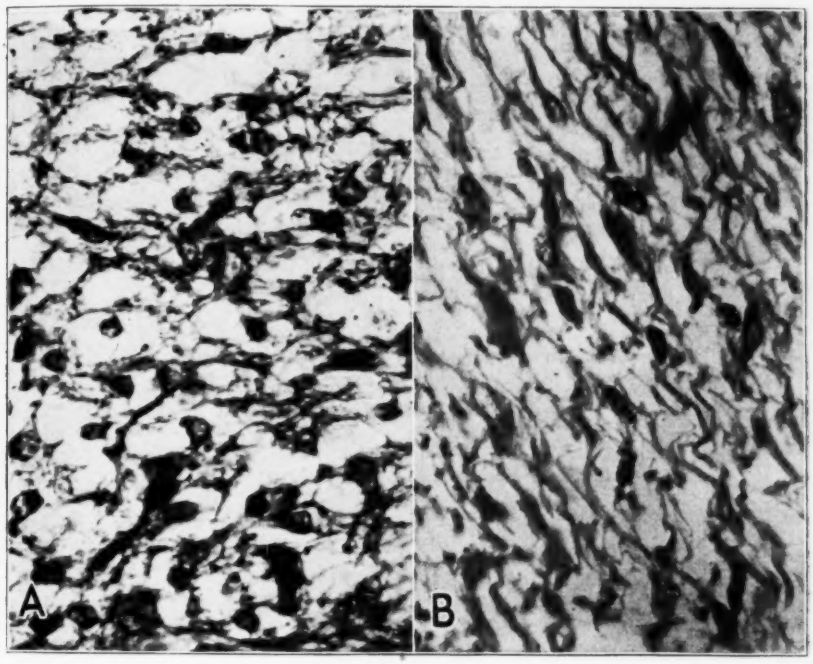

Fig. 11.—Mature type of spongioblastoma polare. *A* (case 10) shows a field of astrocytes. Phosphotungstic acid and hematoxylin (Mallory-Davidoff). *B* (case 10) shows an area of polarized spongioblasts from the same tumor. The wavy processes give a close resemblance to elastic tissue. The effect is probably due to intercellular edema. Paraffin block fixed in a solution of formaldehyde, deformaldehydized and reembedded after four years. Phosphotungstic acid and hematoxylin (Mallory-Davidoff).

of polarized spongioblasts (fig. 11 *B*), which are arranged in streams of parallel cells. In some sections both kinds of cells occur in large numbers, and transitional forms of all kinds are seen. Like the other types, these tumors infiltrate between nerve bundles, and many ganglion cells remain embedded in the tumor.

CLINICOPATHOLOGIC CORRELATION

Clinically, there was little difference in the behavior of patients with the three types of tumor (table of cases). In one particular, however, the course differed considerably. The inevitably fatal outcome was reached earlier after the appearance of the initial symptom in patients

Table of Cases

Case	Age on Admission	Period of Survival After Appearance of First Symptom, Months	Initial Symptoms	Signs of Increased Intracranial Pressure	Cranial Nerve Palsies	Involvement of Pyramidal Tract	Cerebellar Signs	Type of Spongioblastoma Polare
1	9	3	Generalized convulsions; left internal strabismus	Marked	Multiple; bilateral	Bilateral	None	Primitive
2	4	1¼	Vomiting; headache; inability to hold up head; staggering; deviation of eyes to left	None	Multiple; left-sided	Left-sided	Present	Primitive
3	3½	¾	Staggering	None	Impossible to determine	Left-sided	Present (history)	Primitive
4	29	3½	Diplopia; right eye turned in	None	Multiple; right-sided	Left-sided	Present	Primitive
5	5	14	Difficulty in looking up; unsteady gait	Marked	Only bilateral weakness of sixth nerve	Bilateral	Present	Pure
6	19	10	Ringing in left ear, followed by deafness	None	Multiple; left-sided	Right-sided	None	Pure
7	35	5¾	Headache; staggering	Marked	Multiple; left-sided	Bilateral; more on left	Present	Pure
8	8	4	Head tilted to right; internal strabismus in right eye	Moderate	Multiple; right-sided	Left-sided	None	Mature
9	4	6	Fall, followed by vomiting	Marked	Bilateral; more on right	Right-sided	Present	Mature
10	4	2	Right eye turned in	None	Bilateral; more on right	Left-sided	None elicited	Mature
11	10	5	Head turned to right; irritability	None elicited	Left-sided	Right sided	Present (history)	Mature

with the primitive type. The longest period of survival in this group was three and a half months. One patient (case 3) died three weeks after the first symptom appeared. On the other hand, the periods of survival in the cases of the "pure" type of tumor were fourteen, ten and five and three-fourths months, respectively, and in those of the mature type four, six, two and five months, respectively.

In this series, spongioblastoma polare appears to be predominantly a tumor of childhood. Only three of the eleven patients were over 10 years of age. This is at variance with the five cases reported by Buckley [14] (and again by Bailey and Eisenhardt [1]), in which the ages

varied from 13 to 59 years. However, the three patients in this series of the pure type of tumor were aged 5, 19 and 35 years, respectively. It is possible, as mentioned previously, that differences in classification account for the discrepancy.

The clinical manifestations presented by the patients in this series are, with few exceptions, readily explained by the anatomicopathologic changes. Of great importance is the tendency of the neoplastic cells to spread along the natural planes between fiber groups, compressing them but not at first interfering with their functions. It is probable that many of these tumors attain a relatively large size before the appearance of any recognizable functional disturbance. In such cases a rapid train of symptoms may be set off by some relatively minor change.

The diffuse nature of these tumors doubtless accounts for the failure of many of them to cause obstruction of the aqueduct with the resultant hydrocephalus. Only four in this series showed hydrocephalus (information about the ventricles in case 5 is lacking, but it is probable that hydrocephalus was present). All the cases except one (case 6) presented the symptoms of increased intracranial pressure. On the other hand, the only apparent explanation for the advanced symptoms of pressure in case 7, with no hydrocephalus, is the actual mass of the huge tumor. Vomiting may not be a symptom of pressure in all cases of pontile tumor, since in three patients (cases 4, 8 and 10) there was severe vomiting without choked disks or hydocephalus, though vomiting occurred in nine of the remaining eleven cases and was not recorded in one of the remaining two. In some cases it was probably a manifestation of direct irritation of the lower part of the brain stem rather than of general pressure.

Involvement of the cranial nerves occurred in every case (in case 3 the patient was not examined), and in eight of the nine cases in which the tumor involved one side of the brain stem more than the other the cranial nerve palsies were predominantly on the side of greater involvement. In case 2 the palsies occurred on the side opposite the greater portion of the tumor, doubtless owing to the almost complete compression of the basis pedunculi high above the nuclear level. The emergence of the sixth nerve on the ventral aspect of the pons, usually occupied by a tough, lobulated mass of tumor (figs. 1 and 2), and the likelihood of strangulation of the sixth nerve by lateral branches of the basilar artery (Cushing [15] and Buckley [14]) account for the sixth nerve palsies in some of the nine cases in which it ocurred, but in others the nerve or its nucleus was actually involved in the tumor. Bilateral sixth nerve paralysis, which occurred in four cases in this series, is almost always definite evidence of an intrapontile lesion, as has been emphasized by

15. Cushing, H.: Strangulation of the Nervi Abducentes by Lateral Branches of the Basilar Artery in Cases of Brain Tumor, Brain **33**:204, 1910.

Sachs.[16] As Sachs stated, it is strange that the seventh nerve is not also bilaterally involved as its fibers curve about the sixth nucleus, but this occurred in only one case. The fact that definite involvement of the eighth nerve was demonstrated in only three cases is doubtless due to the age, lack of cooperation and poor condition of many of the patients, as in a number of cases the eighth nerve was involved in the lesion. The third nerve was involved in only three cases in this series, while twelve of the fifteen patients with pontile tumors reported by Horrax[17] showed third nerve palsy. In the three cases in this series the tumor extended high into the upper part of the brain stem and undoubtedly involved the nuclei of the third nerve (fig. 1). The eleventh and twelfth nerves were involved by all four mature tumors, but by only three of the remaining seven. In all cases the symptoms were readily explained by the anatomic findings.

In case 5, the only cranial nerves involved were the sixth. At necropsy, however, this tumor, unlike the others, arose from the pars dorsalis of the pons and did not involve the ventral nuclei. The region in which the nuclei of the sixth nerves lie was completely obliterated by the tumor.

Involvement of the pyramidal tract was found in every case. It was bilateral in three cases and was on the side opposite the area of greatest tumefaction in seven others. In case 9 it occurred on the side on which the cranial nerves were most involved. This is readily explained by the bilateral location of the tumor (as described in the report given of the necropsy).

Cerebellar signs (nystagmus, ataxia and staggering) were present in seven cases. Whether they were due to invasion or compression of the cerebellum or to interference with the projection paths to and from the cerebellum in the brain stem it is impossible to state, since the opportunity for both factors to play a part was present in most of the cases in this series. True irritative cerebellar fits were not observed in any case. Other types of focal irritative phenomena were observed in three cases, however, and in case 1 there were two generalized convulsions.

In only one instance (case 2) was there definite evidence of involvement of the corpora quadrigemina. These structures, though readily compressed from above (e. g., by pineal tumors), are rarely involved by tumors of the brain stem.[18]

The gross appearance of these tumors was much the same in all cases. All were of firm consistency. Clinically, the four cases in which cysts were found in the tumors did not differ from the others,

16. Sachs,[13] p. 271.

17. Horrax, G.: Differential Diagnosis of Tumors Primarily Pineal and Primary Pontile, Arch. Neurol. & Psychiat. **17**:179 (Feb.) 1927.

18. Horrax.[17] Bailey,[6b] pp. 328 and 332.

save that the cystic areas usually corresponded with the first localizing symptoms to appear and hence represented the probable point of origin of the tumors.

Clinically, spongioblastoma polare differs little, if at all, from the other gliomas of the pons.[14] Its relatively slow growth is of little advantage in so unfavorable an anatomic situation. The pontile gliomas are uniformly fatal.

Since tumors of the pons are not amenable to surgical treatment, localizing diagnosis is of great importance. The most valuable diagnostic criterion has been said to be the initial symptom complex, which is characteristically the slow development of cranial nerve palsies and the absence or late appearance of intracranial hypertension.[19] In the present series (table), however, five cases presented early symptoms of increased pressure, and only seven showed involvement of the cranial nerves in the first group of symptoms. Of the latter, one (case 6) presented the characteristic history of tumor of the eighth nerve (a not uncommon finding in pontile tumors [20]), and in five of the others the first cranial nerve palsy was of the sixth, a notoriously unreliable sign.[21] Fortunately, with the progression of the lesion the picture sometimes becomes more characteristic (case 2). In cases with well defined cerebellar symptoms the surgeon is often faced with the necessity of intervening surgically in the hope that the lesion is primarily cerebellar.

SUMMARY

The clinical and pathologic observations in eleven cases of pontile tumors classified as spongioblastoma polare have been presented.

It has been pointed out that this group of tumors is essentially transitional. I have therefore included in it not only the pure tumors composed entirely of polarized spongioblasts, but also the transitional forms between the pure type and the spongioblastoma multiforme on the one hand and the astrocytoma on the other. The criteria of classification have been the presence of large numbers of polarized spongioblasts and the absence of evidence of rapid growth.

The clinical behavior has been found essentially the same, regardless of the type of tumor.

An attempt has been made to explain the symptoms presented on the basis of the functional disturbance of the anatomic areas involved by the tumors.

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19. Bailey,[6b] p. 325. Horrax.[17] Sachs,[13] p. 271.

20. Horrax, G., and Buckley, R. C.: A Clinical Study of the Differentiation of Certain Pontile Tumors from Acoustic Tumors, Arch. Neurol. & Psychiat. **24**:1217 (Dec.) 1930.

21. Cushing.[15] Sachs,[13] p. 271.

INTRAMEDULLARY TUMORS OF THE BRAIN STEM

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Tumors originating in the brain stem and limited almost exclusively to this structure are decidedly less common than tumors in other portions of the brain, as shown by the records of the Neurological Institute of New York and those of Dr. Cushing's clinic. The records of the Neurological Institute for the past eight years show that of 432 pathologically verified neoplasms of the brain only 7 involved the brain stem particularly. In 16 additional patients admitted to the Neurological Institute during the past two years a clinical diagnosis of intra-axial neoplasm was made but not verified by autopsy. Of a total of 1,737 tumors of the brain of all types verified in Dr. Cushing's clinic up to April 1930, 25 were pontile gliomas (Buckley).[1] In the group of 782 unverified tumors of the brain, a similar diagnosis was made in 28 instances.

The clinical recognition and localization of an infiltrating tumor in a structure such as the brain stem offer, theoretically, at least, little difficulty. In this situation, where many centers of function of the nervous system are confined within a small space, one expects definite localizing signs. Unfortunately, this is not always the case, and consequently many problems of localization arise when the patient is examined. This is evidenced by the fact that in a number of the patients an operation, often exploratory in nature, is performed. If the diagnosis of a glioma of the pons or medulla were clear, such a procedure would not be attempted. In many cases, on the other hand, the correct diagnosis can be made without especial difficulty.

The differential diagnosis between a tumor and any other disease affecting the brain stem offers greater difficulty than that of the localization of the lesion. It is often clear that the pathologic process is in the brain stem, but the clinical picture produced by a tumor may be bizarre,

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1. Buckley, R. C.: Pontile Gliomas, Arch. Path. **9**:779 (April) 1930.

and the symptoms may be very similar to those of a degenerative or inflammatory process. This was well shown in the 5 cases reported by Brock and Needles [2] in which the patients were studied by various neurologists and in which the diagnosis as to the nature of the lesion that was made during the earlier stages of the illness was later found to be incorrect. In all of the cases the first diagnosis was degenerative, inflammatory or vascular disease. In 3 cases the correct diagnosis was made at a later date. In our 7 cases similar errors in diagnosis were made during the early part of the patient's illness.

REPORT OF CASES

The following records of our cases demonstrate some of the diagnostic difficulties that were encountered. Postmortem studies made it possible to correlate the clinical syndromes during life with the size and character of the neoplasms found at autopsy.

CASE 1.—*Symptoms of five years' duration. Spastic quadriplegia, sensory changes and muscular incoordination. Impaired function of the fifth, seventh, eighth, ninth and tenth cranial nerves. Polar spongioblastoma of the medulla, pons and upper cervical cord.*

History.—A girl, aged 8 years, was admitted to the Neurological Institute, in the service of Dr. Foster Kennedy, on March 10, 1932. Birth had been uncomplicated, and development had been normal up to the age of 3 years. During the ensuing twelve months the parents observed that the child fell backward when standing or walking, and that she frequently complained of pain in the occipital and cervical regions. During the following three years she became increasingly weak and awkward in the use of the hands and feet. The pain in the occipital region continued intermittently, although it did not increase in severity. When the child was 6, she was no longer able to stand or sit upright. At the age of 7, a tonsillectomy was performed because of difficulty in breathing and swallowing; it was followed by slight improvement in a few symptoms. During the ensuing year the patient lost almost all power in the upper and lower extremities, her voice became high pitched, and she lost a great deal of weight.

An examination of the child at the age of 4, one year after the onset of the symptoms, revealed muscular incoordination and rigidity of the musculature of the back of the neck. A diagnosis of osteomyelitis of the cervical vertebrae was made by the physician in charge.

At the age of 7, an examination at a second hospital revealed the presence of an incomplete spastic quadriplegia, with signs of marked involvement of the pyramidal tract and of diminished sensitiveness to pin-prick over the right half of the body. There were marked muscular incoordination of the hands and feet, inconstant nystagmus on looking to either side and flattening of the left facial musculature; hearing was diminished in the left ear. The vestibular responses to warm water were more active on the right side. The tongue protruded to the left, and the corneal reflex on the same side was diminished. The optic fundi appeared to be normal.

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2. Brock, Samuel, and Needles, William: Tumors of the Brain Stem: A Clinical Study of Five Cases with Autopsy Findings, J. Nerv. & Ment. Dis. **72**:521 (Nov.) 1930.

Four months later the patient was admitted to the Neurological Institute. She was markedly emaciated and somewhat cyanotic, owing to respiratory embarrassment. There were complete spastic quadriplegia, signs of marked bilateral involvement of the pyramidal tract and right hemihypalgesia which included the lower two thirds of the face. The neck was held rigid, and attempted flexion of the head caused pain. There was tenderness over the upper cervical vertebrae. Examination of the cranial nerves showed pallor of the optic disks without papilledema, nystagmus on lateral gaze, deviation of the jaw to the right and weakness of the right facial muscles. The tongue was protruded in the midline. The voice was high-pitched, and speech was dysarthric. Movements of the diaphragm were apparently absent. The patient died of respiratory failure on the day after admission to the hospital.

Autopsy.—The cerebral hemispheres showed slight evidence of a previously increased intracranial pressure, and there was slight dilatation of the lateral and third ventricles and of the aqueduct of Sylvius. The entire medulla oblongata and the upper cervical segments of the spinal cord were infiltrated by a large, irregular tumor measuring 7 cm. in length and 5 cm. in width at its broadest point (fig. 1). It was firm in its caudal fourth, where it caused an enlargement of the medulla and cervical cord but allowed them to retain their general shape. Farther cephalad in the tumor mass there were two cysts which extended asymmetrically to the left (fig. 2). The larger, posterior and more lateral of the two cysts pressed deeply into the inferior surface of the left lateral lobe of the cerebellum.

On section of the stem it was noted that the tumor had almost obliterated the posterior half of the fourth ventricle, while the anterior half was slightly dilated. The tumor mass extended upward to a point about 2 mm. below the eminentiae abducentis. In the uppermost portion it involved mainly the left side of the medulla to the border of the inferior olive. Below, the growth had diffusely invaded the entire stem; the inferior olives, pyramids and medial fillets were just visible through the white, somewhat glassy-looking tumor tissue. The tumor was seen to extend into the pia below the pyramids for a distance of 3 mm. The cerebellar gyri on the inferior surface of the left lateral lobe were somewhat flattened from the pressure of the cystic, bulging portion of the tumor. The two upper cervical segments of the spinal cord were grossly infiltrated by neoplastic tissue, and the gray matter could be seen only in faint outline down to the seventh cervical segment.

Microscopic Studies: The tumor was rather well defined; it was vascular and hyperemic at its margins and degenerated and cystic in its center. At the periphery the neoplasm was moderately cellular and fibrillar, the fibers forming a loose meshwork. The cells were elongated and bipolar for the most part and had a tendency to lie in parallel formations. Many of the "fibers" were found to be the long processes of these bipolar cells; often they were thick, homogeneous, undulating and corkscrew-like. In addition, there were a few unipolar cells and large, angulated cells with multiple fibrous processes (fig. 3).

Comment.—The fact that the patient lived five years after the first appearance of symptoms is remarkable. Other instances, however, have been reported in which patients lived even longer than this. Confusing factors in this case were the pain in the cervical region and the rigidity of the neck, which led observers to suspect a disease of the cervical vertebrae. Two other patients in our group complained of similar pain.

The fact that the optic disks appeared normal four years after the onset of the illness was unusual and made the diagnosis of tumor of the brain difficult. Even during the last stages of the illness the clinical syndrome was not so clearly outlined as one might have expected, for the general signs of tumor of the brain were lacking even at this time. The size of the neoplasm as seen at autopsy

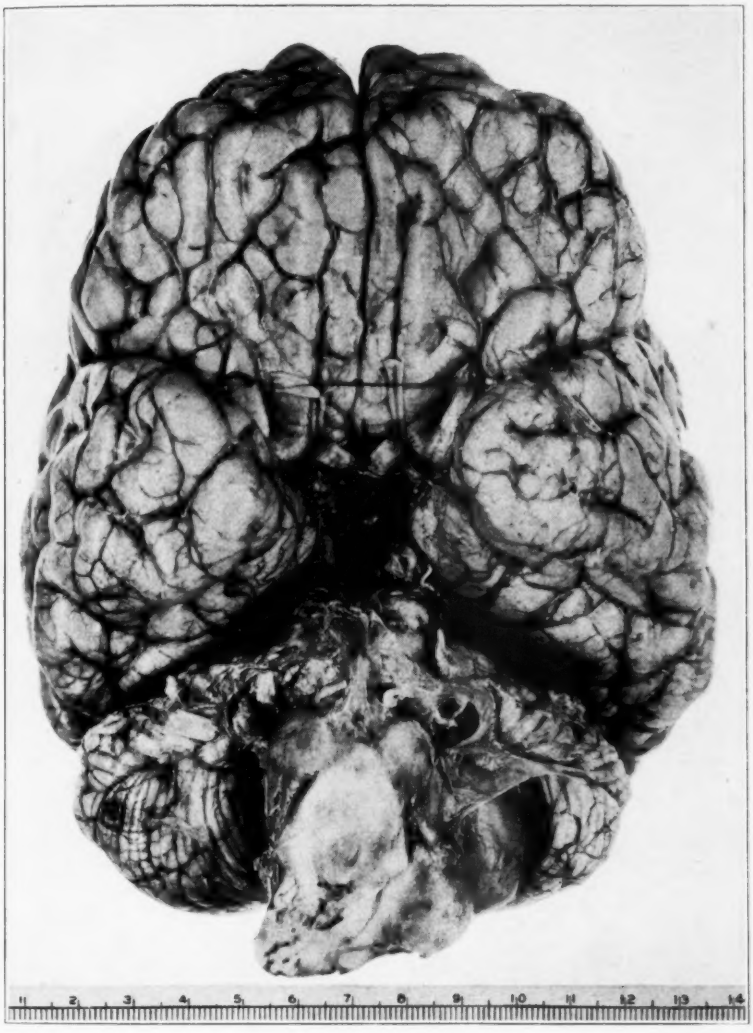

Fig. 1 (case 1).—A large polar spongioblastoma in the pons and medulla.

appeared entirely out of proportion to the severity of the symptoms. Judging from the gross appearance of the tumor one might have postulated a cessation of function of most of the structures in the pons and medulla, although clinically many of the cranial nerves and projection pathways through the stem had been found to function well.

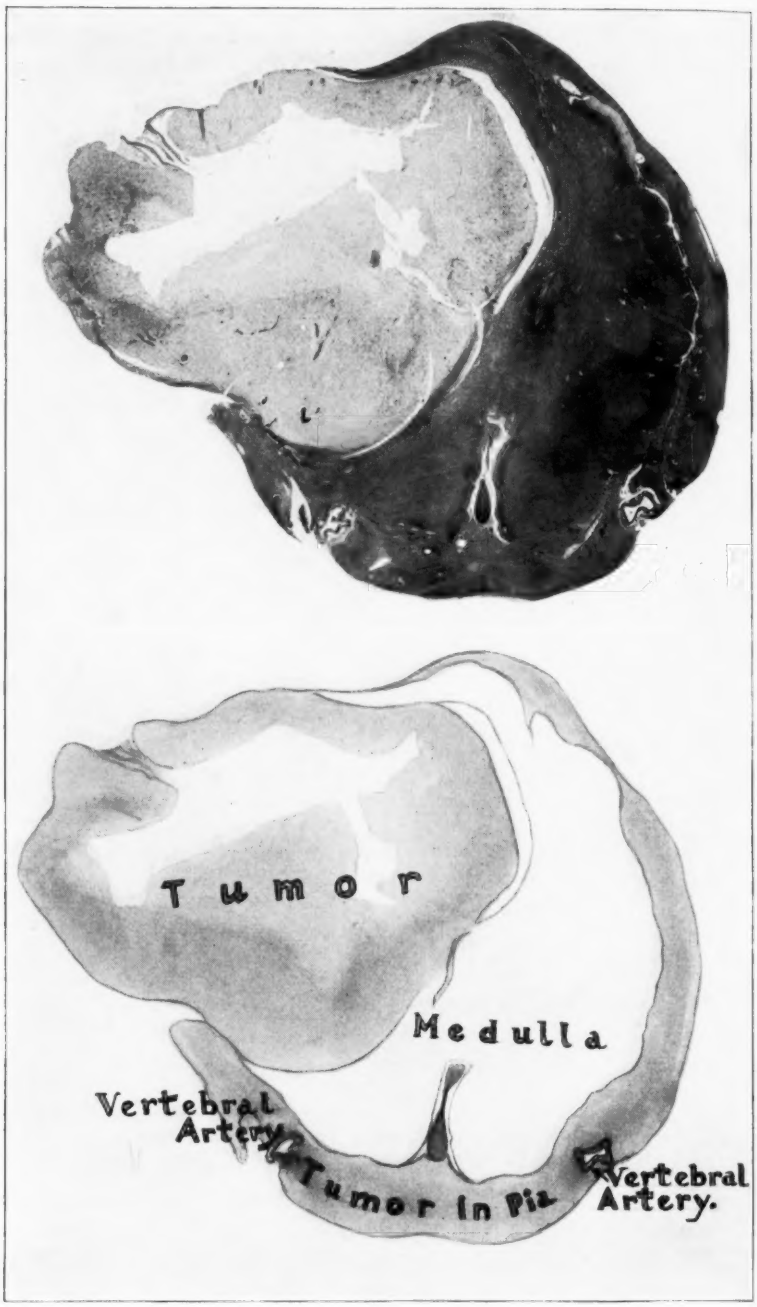

Fig. 2 (case 1).—*A*, cross-section of the medulla, showing a cystic tumor and invasion of pia-arachnoid. *B*, diagram of figure 2 *A*.

The tumor was a polar spongioblastoma, a type known to grow slowly, which explains the long clinical history. Although recently the polar spongioblastomas have come to be considered among the most common tumors of the brain stem, we have encountered only one in our small series.[3] In his large group of tumors of the brain stem Buckley described a preponderance of tumors of other types, and our observations corroborate his statements.

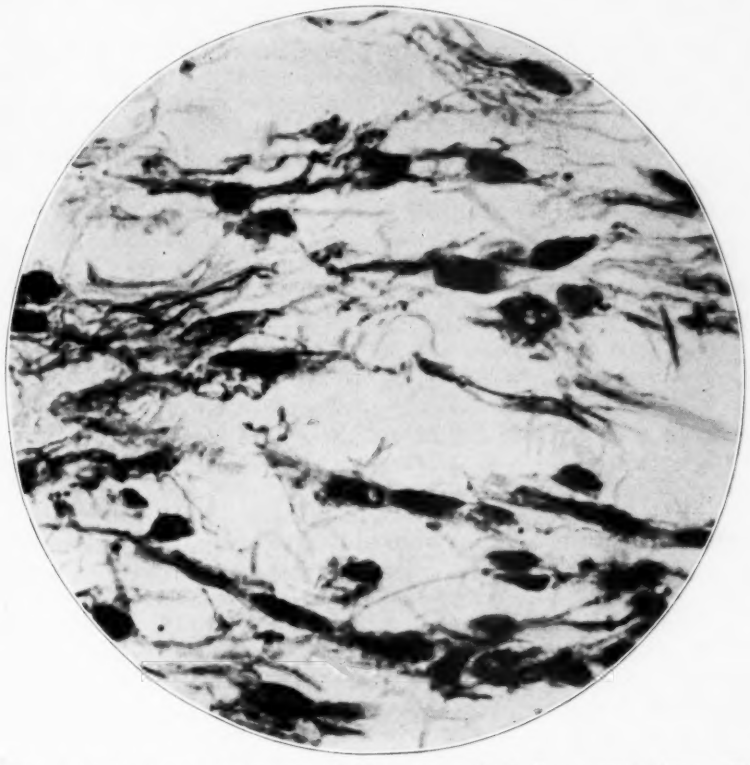

Fig. 3 (case 1).—A polar spongioblastoma and bipolar spongioblasts. Phosphotungstic acid; × 250.

CASE 2.—*Ataxia of all of the extremities. Left hemiparesis. Impaired function of the fifth, seventh and ninth cranial nerves of two months' duration. Glioblastoma multiforme of the pons and medulla.*

History.—A girl, aged 6 years, was apparently well until Aug. 21, 1925, when she became suddenly dizzy and walked about in a circle for almost three minutes, the body turning to the left. The eyes likewise were turned to the left during the attack, and at its termination she vomited once. The attacks were repeated daily for several weeks, following which vision began to fail, and the child was

3. Since this paper was completed, 2 other cases of polar spongioblastoma of the brain stem have come to autopsy.

unable to walk because she could not control the movements of the lower limbs. The head was held to the left, and at times she complained of pain in the back of the neck.

Examination.—The patient was admitted to the Neurological Institute in the service of Dr. Frederick Tilney on October 2, approximately two months after the beginning of the illness. Lack of cooperation prevented a complete neurologic examination. The child was somewhat somnolent and lay in bed with the head turned to the left. There were marked ataxia in all of the extremities, more on the left, left hemiparesis and increase of tendon reflexes on the left, with a bilateral Babinski sign and confirmatory signs. The results of the sensory examination were not reliable. The pupils were equal and contracted to light and in accommodation, but there was paresis of the external rectus muscles. The optic disks appeared normal. The right side of the face was weaker than the left; the pharyngeal reflex was absent on both sides, and there was difficulty in swallowing and in speech.

Roentgen studies of the skull and laboratory tests showed no abnormalities. A trephine opening in the right posterior parietal region revealed a pulsating dura, and a needle passed into the right lateral ventricle showed that the fluid was under normal pressure.

Course.—During the three weeks in the hospital the patient was semistuporous; she became progressively weaker and died apparently of medullary compression.

Autopsy.—There was definite asymmetry of the stem, the right half of the pons and the right middle cerebellar peduncle being somewhat larger than the left. The left olivary body was approximately twice the size of the right and had a somewhat nodular surface. The right cerebellar hemisphere was displaced laterally. It bulged upward into the fourth ventricle, forming a large hillock in the floor of the ventricle and almost completely obstructing it. Only the posterior third of the medullary portion of the floor of the fourth ventricle retained its normal landmarks and contours. The tumor mass was approximately spherical, 3.5 cm. in diameter, with indistinct margins, homogeneous and yellowish gray. On section it was seen to extend into the depths of the cephalic two thirds of the right side of the medulla. In this area none of the normal medullary structures could be seen while on the left the inferior cerebellar peduncle and pyramidal tract could still be recognized. The tumor extended into the right two thirds of the reticular portion of the pons. In the latter area, the transverse fibers and pontile nuclei were obscured and replaced by homogeneous gray tumor tissue.

There was a small, separate, well demarcated tumor nodule in the lateral portion of the left side of the tegmentum of the pons and the lower portion of the tegmentum of the midbrain, which measured approximately 9 mm. in diameter and was grayish, granular and soft.

The left olive was larger than the right, paler and less definite in its markings, as if it were diffusely infiltrated by tumor tissue. The aqueduct was moderately dilated, and there was moderate dilatation of the third and lateral ventricles. The medial surface of the left hemisphere of the cerebellum was compressed by the large tumor of the stem. The cerebral hemispheres were symmetrical, but there were moderate flattening of the gyri and narrowing of the sulci over the hemispheres.

Microscopic Studies: The tumor was cellular, the cells varying considerably in size, shape and nuclear type. There were many small cells with scant cytoplasm and spherical, deep-staining nuclei. There were elongated cells with unipolar and bipolar processes of varying thickness and with oval nuclei. Some of the cells

had oval or spherical bodies with one or more processes and one or more spherical or oval nuclei, which were rather vesicular, while others were stellate and polygonal and had true fibrous processes. There were many multinucleated giant cells. In a number of zones the giant cells predominated. Special stains showed that the cells just described belonged to the glial series.

Comment.—The general appearance and semistuporous state of the patient were similar to the symptoms seen in patients with greatly increased intracranial pressure, but there was no papilledema, and exploratory puncture revealed that the intracranial pressure was not increased. The signs in this patient were consonant with those of a lesion localized in the brain stem, although the prominence of the cerebellar ataxia made that diagnosis uncertain. It was surprising with so extensive a lesion in the pons and medulla that so few of the cranial nerves were involved. The well known fact that most patients with neoplasms in the brain stem withstand any operative procedure poorly was borne out in this case.

The tumor was a glioblastoma multiforme. This is a tumor which grows rapidly—a fact consistent with the short clinical course. Glioblastomas are ordinarily found in the middle decades of life, whereas this patient was 6 years of age. It is interesting to note that in Buckley's series of gliomas of the pons, 7 of the 10 tumors diagnosed as glioblastoma multiforme occurred in children.

CASE 3.—*Symptoms of six months' duration. Left spastic hemiplegia, nystagmus, left facial paresis and difficulties in speech. Astrocytoma fibrillare of the medulla, pons and midbrain extending into the right thalamic region.*

History.—A girl, aged 6 years, was admitted to the Neurological Institute, in the service of Dr. Walter Timme, on June 30, 1931. She had been well until six months before, when tonsillectomy was performed. One week later paralysis of the left side of the face developed. Four months later the left arm became weak, and shortly thereafter the left leg was partially paralyzed.

The child was able to walk, although she dragged the affected leg. About one month before admission she had a convulsive seizure involving the left side of the body, and thereafter marked difficulty in speech gradually developed. This was accompanied by inability to close the right eye and marked limitation of the movements of the eyeballs in all directions.

Examination.—The patient was stuporous and, although she could be aroused, cooperation was poor. The postural attitude was that of left hemiplegia. Equilibratory and nonequilibratory tests could not be carried out. The tendon reflexes were definitely increased on the left side of the body, and dorsal extension of the toe on that side occurred on plantar stimulation. The pupils were round and equal, and reacted promptly to light. The optic disks showed papilledema of 3 diopters, with retinal hemorrhages. There were spontaneous nystagmus and paralysis of the left facial muscles. The remaining cranial nerves could not be tested.

Course.—The child died the day after a right, subtemporal decompression had been carried out as an emergency measure because of her alarming condition.

Autopsy.—A large tumor was present in the pons, extending into the right cerebellopontile angle. Its shape was asymmetrical, and it extended chiefly to the right, so that the right middle cerebellar peduncle was much larger than the left.

The mass, approximately 3.5 cm. by 3 cm., was ovoid and lay chiefly in the anterior third of the right side of the medulla and the right side of the pons (fig. 4). It bulged outward into the right middle cerebellar peduncle, which indented the medial aspect of the adjacent right cerebellar hemisphere. The

growth extended somewhat into the left side of the stem and caused an upward bulging of the floor of the fourth ventricle, almost obliterating it. It extended into the right side of the midbrain and compressed the aqueduct of Sylvius to a marked degree. The tumor was grayish and somewhat soft and had indefinite margins. In its pontile portion there were softened granular areas. Through the right middle cerebellar peduncle a small finger of tumor extended into the medial portion of the central white matter of the right cerebellar lobe. Tumor tissue was seen extending in a patchy fashion into the right pulvinar of the thalamus, the hypothalamus and the medial portion of the main body of the thalamus. Both lateral ventricles showed a considerable degree of internal hydrocephalus, especially in the inferior horns.

Microscopic Studies: The tumor was only moderately cellular, being composed chiefly of a loose-meshed, fibrous mat. The cells were large, polygonal, stellate,

Fig. 4 (case 3).—A fibrillary astrocytoma in the pons extending asymmetrically to the right.

elongated or irregular and homogeneous or finely granular, having long fibrous processes and large vesicular nuclei. Among them occasional well preserved or degenerating ganglion cells were found. There were numbers of microglia, compound granule cells and occasional oligodendroglia. With special stains the tumor cells were shown to be fibrous astrocytes. There was evidence of amitotic division, but no mitoses were seen. At the margins of the tumor there was mild gliosis. The surrounding stem and thalamus were slightly edematous.

Comment.—The first symptom (facial paralysis) noted in this case was of a localizing nature, though symptoms of intracranial pressure developed after a short time. The convulsive seizure was probably the result of the neoplastic extension upward into the thalamic region. Operative procedure apparently hastened the fatal termination only a little in this case, as it was utilized merely as an emergency measure.

The tumor was a fibrillary astrocytoma which, unlike that in case 1, was solid, and the clinical history was comparatively short. In one of the 6 fibrillary astrocytomas among Buckley's pontile gliomas the clinical history was of only six months' duration. That the obstruction of the fourth ventricle gave rise to an early, more intensive hydrocephalus in this case probably explains the difference in duration between this and case 1. This tumor extended into the right cerebellopontile angle, but did not produce a syndrome typical of a growth in that location. Of Buckley's total of 9 astrocytomas, 5 were suspected of being acoustic tumors.

CASE 4.—*Symptoms of four months' duration. Ataxia of all of the extremities, signs of the bilateral involvement of the pyramidal tract, right hemihypesthesia, early papilledema and impaired function of the fifth, sixth, eighth, ninth, tenth, eleventh and twelfth cranial nerves. Glioblastoma multiforme of the medulla.*

History.—A boy, aged 6 years, who was admitted to the Neurological Institute as a patient of Dr. C. A. Elsberg on Sept. 4, 1926, had been well until June 1926, when the left eye was observed to be turned inward. There were no other symptoms until August 1926, when there developed awkwardness in gait and indistinctness of speech. This was followed in about ten days by awkwardness in the use of the right hand, difficulty in swallowing and generalized failure of muscular strength combined with loss of weight. Early in September, the boy complained of pain in the head and the back of the neck, which was increased by change in position or by coughing.

Examination.—In September, the child was mentally clear and cooperative. He was unable to sit up or to walk without aid. Gait was unsteady, and he fell to either side or backward. In the nonequilibratory tests marked ataxia was present on each side, that on the right being more pronounced. There was hypotonus of the muscles of all of the extremities, and the tendon reflexes were diminished, though positive Babinski, Chaddock and Oppenheim reflexes were elicited bilaterally. Sensation to all of the forms of stimuli was diminished over the right half of the body, including the face and cornea.

The right optic disk presented a picture of a moderate papilledema, with engorged retinal veins. The margins of the right disk were slightly blurred. The pupils were large and equal and reacted promptly to light. The left external rectus was somewhat paretic, and coarse nystagmus to the left was present. There were paralysis of the soft palate, difficulty in swallowing and inability to speak above a whisper. The muscles supplied by the spinal accessory nerves were weak bilaterally, and although the tongue protruded in the midline, the muscles were uniformly atrophied.

Course.—The patient died about two hours after an exploratory suboccipital operation at which no increase of intracranial pressure was noted in the posterior fossa. Death was apparently due to sudden respiratory failure.

Autopsy.—There was an irregular tumor in the cephalic half of the medulla, measuring approximately 3.5 by 2 by 2 cm. It was directly continuous with the medullary substance and could not be enucleated. It was yellowish gray and showed many hemorrhagic, purplish areas. The tumor mass was firm, and a thin membrane covered its external extension to the left. The surface markings of the cephalic portion of the medulla were considerably flattened and obscured.

On section, the tumor within the medulla measured approximately 2.5 cm. in diameter. It occupied the medullary substance from the lower level of the eminentiae abducentis down to the middle of the hypoglossal nucleus. In the dorso-

ventral direction it extended from just beneath the floor of the fourth ventricle on the right down through the olive. The posterior half of the floor of the fourth ventricle bulged upward to a slight extent. There was, however, no dilatation of the anterior half of the fourth ventricle or of any of the ventricular system anterior to it. The tumor pressed on both middle cerebellar peduncles. The cerebellum and cerebrum failed to show gross lesions.

Microscopic Studies: The tumor was fairly cellular, and its cells showed the variations described in the tumor in case 2 (fig. 5). Many types of glia cells were represented. Many of the vessels showed endarteritis; quite a few were

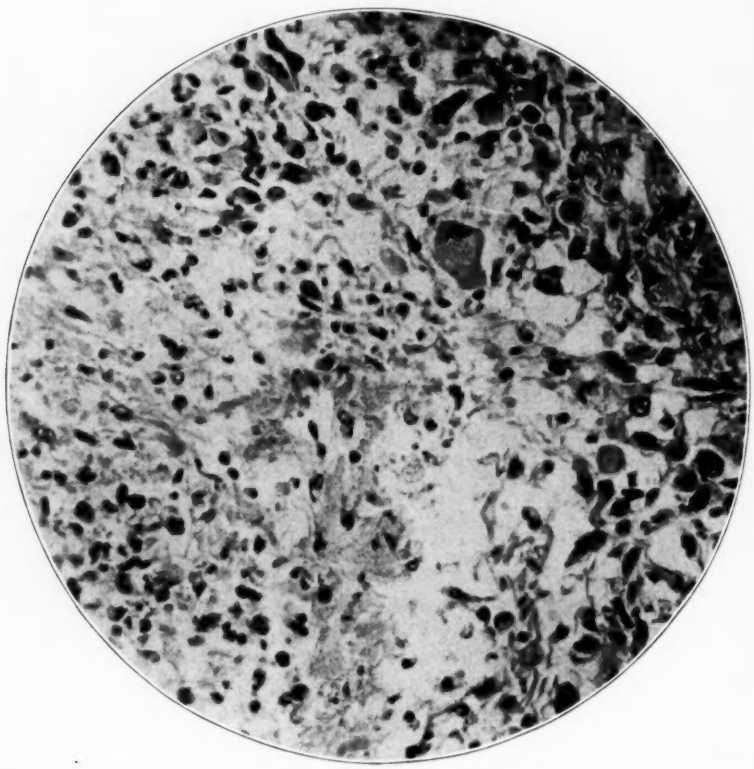

Fig. 5 (case 4).—Glioblastoma multiforme, showing cell variation. Hematoxylin-eosin; × 250.

thrombosed, and there were scattered zones of necrosis. There were a number of pseudopalisades. In some areas the protoplasmic astrocytes predominated.

Comment.—Most of the functions of the cranial nerves were involved in this case, and cerebellar signs were prominent. Careful consideration of the clinical signs led to the diagnosis of a cerebellar tumor or a tumor of the brain stem. An exploratory operation on the posterior cranial fossa was therefore considered advisable; if a tumor had been found outside the stem the patient might have been greatly benefited.

Anatomically, the tumor extended through an area which would well account for all of the symptoms, though it is remarkable that more disturbances were not present.

The neoplasm was a glioblastoma multiforme and, as in a previous case with a tumor of the same type, the clinical history was short. Here again the patient was a child, although glioblastomas elsewhere in the central nervous system are more common later in life.

CASE 5.[4]—*Symptoms of three months' duration. Bilateral papilledema and contracted visual fields. Slight cerebellar signs. Astrocytoma fibrillare beneath the floor of the aqueduct of Sylvius, with obstructive hydrocephalus.*

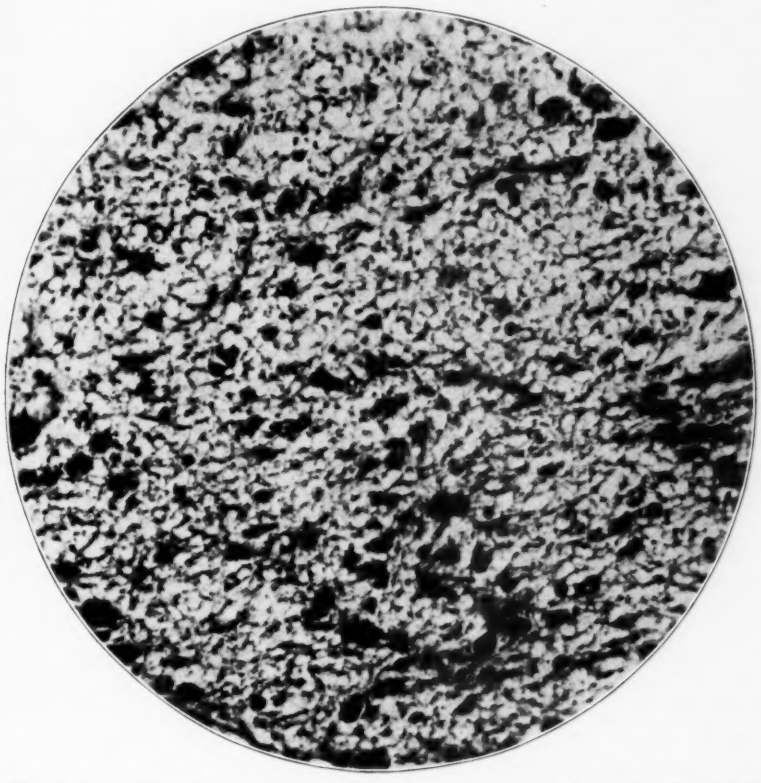

Fig. 6 (case 5).—Astrocytoma fibrillare. Phosphotungstic acid stain; × 500.

History.—A boy, aged 9, who was admitted to the Neurological Institute, in the service of Dr. Walter Timme, on March 20, 1930, had had the first symptoms of illness apparently about three months before. He began to wet the bed and also to get up to urinate three or four times each night. He gained rapidly in weight from this time and suffered from frequent headache. The first observation concerning vision occurred about two months later, when he was sent home from school with a request from the teacher for an examination of the eyes.

4. This case was previously reported by Dr. S. T. Orton (A Clinical and Pathological Study of Two Cases of Obstruction of the Aqueduct of Sylvius, Bull. Neurol. Inst., New York **1**:78, 1931). Dr. Orton permitted us to report the case again.

The physique was of the pituitary type. Slight disturbances of cerebellar function were recorded by some observers, and the tendon reflexes were diminished but not abnormal. Papilledema of 2 diopters was present in each optic disk, and the visual fields were contracted with a tendency toward binasal hemianopia. Vestibular tests were interpreted as indicative of a supratentorial lesion. Roentgenograms of the skull showed marked separation of the sutures and enlargement of the sella turcica.

Ventricular puncture yielded fluid under a pressure of 240 mm. of water. Roentgenograms following the injection of air into the lateral ventricles were unsatisfactory. The spinal fluid pressure was 410 mm. of water.

Course.—The patient was operated on at an early date because of rapidly failing vision. Exploration of the chiasmal region of the brain failed to reveal a tumor, though the third ventricle was considerably dilated and pressed on the optic nerves. The patient died about four weeks after the second stage of the operation.

Autopsy.—The cerebral hemispheres were symmetrical and showed generalized flattening of the gyri and narrowing of the sulci. On section of the cerebrum, extensive dilatation of the lateral and third ventricles was noted. Their ependymal lining showed many fine granulations. The fourth ventricle was not dilated. The aqueduct of Sylvius was markedly narrowed, and there was a short space in which no opening could be seen with the naked eye but in which the site of the canal was represented by a translucent, gray, circular area. The gray color also extended for some distance into the tissues below and on either side of the aqueduct; this area was distinctly firmer on palpation than the surrounding tissues.

Microscopic Studies: The aqueduct of Sylvius was almost completely filled by a loose-meshed glial web containing many nuclei. The glial mass pressed upward from the floor of the aqueduct and was composed of a tangled mat of glia fibers, fairly rich in consistently angulated cells which showed a slight amount of cytoplasm and a wide range of active nuclear pictures (fig. 6). All of the essential nerve structures had disappeared from the center of this area. At the edges of the glial mass there was apparently active infiltration into the gray matter and the white matter, and no distinct line of demarcation was present between this and the normal tissue.

Comment.—The symptoms complained of by the patient were chiefly referable to pituitary dysfunction. The signs in the eye were those common to cases of increased intracranial pressure. The position of the neoplasm about the aqueduct of Sylvius resulted in obstructive hydrocephalus of the lateral and third ventricles, and the symptoms and duration of the illness were dependent chiefly on this condition. The tumor was a fibrillary astrocytoma, which ordinarily runs a long course, but its unfortunate position in this case resulted in the rapidly fatal termination.

CASE 6.—*Symptoms of two years' duration. Ataxia of all of the extremities and signs of bilateral involvement of the pyramidal tract. Bilateral papilledema and nystagmus. Hydrocephalus. Astrocytoma fibrillare about the aqueduct of Sylvius.*

History.—A girl, aged 16, who was admitted to the Neurological Institute, in the service of Dr. Walter Timme on Feb. 19, 1931, had had the first symptoms of illness—unsteadiness in walking—about two years before. This difficulty, with a slight dragging of the right leg when she walked, slowly progressed until November 1932. About this time symptoms of intracranial pressure developed, consisting of occipital headache and vomiting. Relief from the headache was

obtained by retraction of the head. Two months later drowsiness, combined with exaggeration of the symptoms of pressure, resulted in admission of the patient to the institute.

During the two years prior to the onset of the symptoms noted, the patient's head gradually enlarged, and there was a definite change in mental ability. Symptoms of pituitary dysfunction had been present for the same period.

Examination.—The head was markedly enlarged, measuring 60 cm. in circumference, and there was a cracked-pot resonance on percussion. The girl was bedridden and stated that when she attempted to stand her legs crumpled under her. Coordination was poor in all of the extremities. The tendon reflexes were exaggerated equally on both sides of the body, and a Babinski sign was elicited bilaterally. Muscle power was fairly good, but was less on the left side. Definite muscular hypotonia, most marked in the lower extremities, was noted. Papilledema of 4 diopters was present in each optic disk, and the visual fields were concentrically contracted. The other cranial nerves functioned normally. Mentally the patient was dull and concentrated poorly. The intelligence quotient was 80. Roentgenograms of the skull revealed a marked increase of intracranial pressure with a secondarily enlarged sella turcica.

Course.—Operative procedure consisted of puncture of the corpus callosum and suboccipital exploration, which failed to relieve the symptoms or to establish a diagnosis. The patient reacted poorly to this procedure, became gradually more stuporous and died several days after the operation.

Autopsy.—The cerebral hemispheres were symmetrically enlarged. The gyri were flattened, and the sulci narrowed. There were no unusual features to the gyral pattern. There were marked internal hydrocephalus of the lateral ventricles and moderate enlargement of the third ventricle. There were corresponding compression and diminution of the central white matter. The width of the cortex appeared normal.

Externally the cerebellum and brain stem appeared normal. The aqueduct of Sylvius was considerably narrowed, being compressed from above and from both sides. In the roof of the aqueduct was a solid, whitish mass, roughly triangular and measuring approximately 0.4 by 0.5 by 1 cm., incorporated in the corpora quadrigemina. It reached down to the superior medullary velum and up apparently to about the upper margin of the anterior corpora quadrigemina. The fourth ventricle, cerebellum and stem showed no abnormalities aside from a pressure cone on the under surface of the cerebellum.

Microscopic Studies: The small mass in the roof and lateral walls of the aqueduct of Sylvius was fibrillar and contained a considerable number of stellate and angulated cells. The fibers were glial in type, division being of the amitotic type. There was a gradual transition from tumor tissue to surrounding gray and white matter.

Comment.—Many features of this case are similar to those of the preceding one. There were signs of pituitary dysfunction, gradually increasing hydrocephalus and cerebellar involvement. A small fibrillary astrocytoma was present about the aqueduct of Sylvius, with resultant internal hydrocephalus, which had apparently given rise to the majority of the symptoms. The longer duration in this case is more consonant with the slow growth of the type of tumor present, and apparently the block of the aqueduct of Sylvius developed rather slowly.

CASE 7.—*Symptoms of two weeks' duration. Ataxia and weakness of right upper and lower extremities. Subjective sensory diminution on the left side of*

the body and right side of the face. Papilledema of 5 diopters. Involvement of the fifth, sixth, seventh, eighth and twelfth cranial nerves. Glioblastoma multiforme of the pons, with metastases to the meninges.

History.—A boy, aged 8, who was admitted to the pediatric division of the Presbyterian Hospital, in the service of Dr. Penfield on May 3, 1927, had presented the first symptoms of the illness two weeks before; they consisted of blurring of vision and severe headache. These were followed in a week by vomiting and a subjective feeling of numbness beginning in the right hand and arm and finally involving the right leg. The mother had noticed that the left eye turned inward for about a week prior to the patient's admission to the hospital, and that during this time he was drowsy and slept a great part of the time. He complained also of difficulty in hearing.

Examination.—When admitted to the hospital, the child was drowsy, but he awakened easily and cooperated well during the examination. He deviated to the right when walking, and the gait was somewhat ataxic. In the Romberg position he fell backward. Muscular coordination was impaired in all of the extremities, but definitely more so on the right. Motor power on the right side was weaker than on the left, and the tendon reflexes were correspondingly exaggerated and greater on the right. The abdominal and cremasteric reflexes were absent. The Babinski sign was present bilaterally. Results of sensory examinations were repeatedly normal despite the subjective feeling of numbness. There was slight rigidity of the neck. Examination of the eyes revealed papilledema of 4 diopters, paralysis of the left external rectus muscle and corneal anesthesia on the left. The size, shape and reactions of the pupils were normal. The jaw deviated to the left when opened, and right peripheral facial weakness was observed. Hearing was reduced in the ears, and the tongue deviated to the right.

Spinal puncture showed 70 mm. of cerebrospinal fluid pressure in the lumbar sac, the fluid being clear and colorless, with increased globulin content, 40 mg. of protein per hundred cubic centimeters and 46 cells per cubic millimeter (all lymphocytes). Roentgenograms of the skull were normal.

Course.—Suboccipital exploration was performed by Dr. Penfield two days after admission of the patient to the hospital. A cerebellar pressure cone was found, with evidence of a cystic tumor deep in the posterior fossa. The child became somewhat stronger following the operation and was discharged one month later. He returned to the hospital in a month because of continued vomiting and headache. Examination at this time gave essentially the same results as on the previous admission, with the additional factor of inequality of the pupils. A second exploration of the posterior cranial fossa revealed several cysts "in each cerebellar hemisphere." The condition following operation was good until about the sixth week, when the boy became stuporous; he died a week later in a convulsive seizure.

Autopsy.—A nodular, cauliflower-like tumor mass replaced the pons varolii and extended well up into the midbrain just beneath the hypothalamus (fig. 7). On cross-section (fig. 8), many hemorrhagic areas were seen in the neoplasm, which bulged forward and which had grown around the pia so that the vein normally found on the under surface of the pons was buried about 1 cm. beneath the tumor. The growth extended upward and backward into the fourth ventricle, which was quite large. The aqueduct of Sylvius was patent. Posteriorly in the tumor mass was a cyst several centimeters in diameter, filled with gelatinous fluid. In the arachnoid space near the medial sulcus and sylvian fissures there were white, ele-

vated nodules varying from a few centimeters to a few millimeters in diameter. The convolutional patterns of the hemispheres were normal, and the lateral and third ventricles were slightly enlarged.

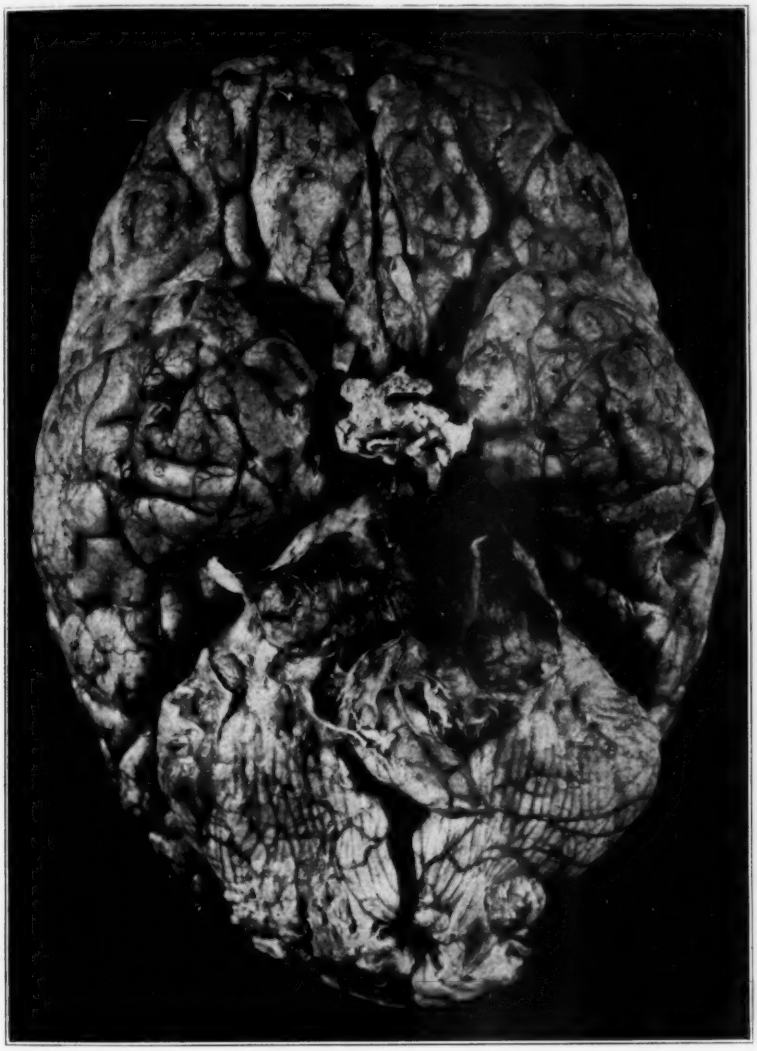

Fig. 7 (case 7).—Glioblastoma multiforme of the pons and midbrain.

Microscopic Studies: The tumor cells were variable in shape and size. A great many were elongated, bipolar and unipolar and had oval nuclei. Many smaller cells had scant cytoplasm and spherical nuclei. Large-bodied spherical, polygonal and stellate cells with one or more processes and spherical or oval nuclei were present. There were occasional multinucleated giant cells, and the blood vessels showed hyperplasia of their intimal lining. Pseudopalisade formations were

found. There were collections of cells in the pia-arachnoid which resembled the cells described in the tumor. These collections correspond with the gross whitish areas described over the cerebral hemispheres.

Comment.—The sudden development of symptoms of increased intracranial pressure was unusual. There were apparently no preceding signs of a lesion in the brain stem, though one suspects that some were present before symptoms were manifested. Clinically, a tumor in the right cerebellar hemisphere seemed more probable than one in the brain stem.

The size of the tumor as seen at autopsy seems out of harmony with the paucity of the clinical signs. It is probable that the hemorrhages into the neoplasm caused the sudden coma with convulsions and death.

Dr. Penfield originally studied the brain in this case, and it was his opinion that the tumor originated in the pons and had metastasized through the spinal

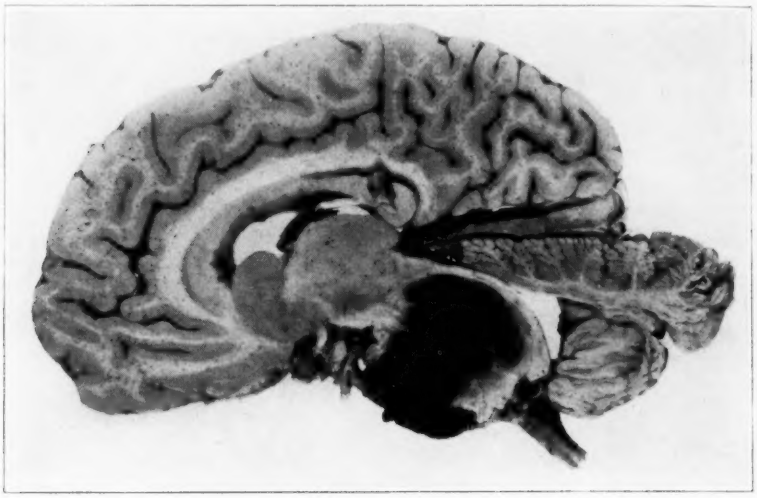

Fig. 8 (case 7).—Glioblastoma multiforme of the pons and midbrain with compression of the cerebellum.

fluid to the cerebral hemispheres on both sides. These metastases were chiefly near the sylvian fissures close to the midline. He believed that this was perhaps an indication of the drainage of the cerebrospinal fluid upward and toward the longitudinal sinus, as there was no evidence of metastases in the ventricles.

The short duration of life in this patient is in keeping with the type of tumor—glioblastoma multiforme.

CLINICAL FEATURES

A comparative study of the clinical features in the 7 cases aids somewhat in the clarification of what one may expect to find in patients with tumors of the brain stem. There can, of course, be no definite syndrome evolved because of the fact that neoplasms may arise at any point in the stem and produce symptoms dependent on the rapidity of the growth and the location. One of the most important factors in the establish-

ment of the diagnosis of a tumor of the brain stem is a study of the manner of onset of the illness. This can be elicited only by taking a careful and complete history.

A description of these earliest symptoms and other clinical factors presented by the 7 cases under consideration follows:

Onset of Symptoms.—In 4 cases, the illness began with localizing symptoms, chiefly signs of involvement of the cranial nerves or disturbances of cerebellar function. In 1 patient the initial symptoms were those of an obstructive hydrocephalus, and in 2 others the illness began with localizing symptoms and evidence of increased intracranial pressure. In 1 case the illness began following tonsillectomy, and in another a similar operation was performed during the course of the illness. The manner of onset in most of these cases is thus quite different from that observed in patients with a neoplasm situated elsewhere in the brain.

Papilledema.—The optic disks in 1 case appeared normal. In a second case, although the optic disks appeared flat, there was evidence that papilledema had been present previously. The optic disks in the remaining 5 cases showed elevation of from 2 to 4 diopters, equal in the two eyes in 4 instances. It is to be remembered, however, that all of the patients were examined during the later stages of the illness.

Cerebellar Signs.—Signs of cerebellar dysfunction were marked in 4 cases, moderately pronounced in 1 case and slightly demonstrable in another. One patient did not cooperate sufficiently to permit proper examination. Cerebellar signs were thus seen to be an outstanding feature in patients with tumors involving the brain stem and were due to disturbed function of one or more of the cerebellar peduncles. In 2 cases the first symptoms noted were referable to cerebellar involvement. This fact causes considerable difficulty in differentiating these tumors of the stem clinically from those localized in the cerebellum.

Pyramidal Tract Signs.—Signs of involvement of the pyramidal tracts resulting from pressure of the neoplasm or direct invasion and destruction were marked in 3 cases. In 2 cases these signs were moderately pronounced and in 1 case slightly demonstrable. In a seventh case these signs were absent. The pyramidal tracts were involved in 1 case to the extent that a quadriplegia existed. In most instances both pyramidal tracts were involved, usually being affected successively.

Sensory Changes.—Two patients had diminished sensibility to pain, touch and temperature over one half of the body. In 3 patients sensibility to external stimuli was normal, and in 2 lack of cooperation prevented proper examination.

Subjective Pain.—Three patients complained of pain localized in the suboccipital or upper cervical area. This was rather severe and was

aggravated by motion of the head. In 1 instance it was so marked that a diagnosis of cervical caries was made in several hospitals.

Cranial Nerve Signs.—Function of the olfactory, oculomotor and trochlear nerves was normal in all of the patients.

Signs of involvement of the trigeminal nerve were found in 3 cases. In 2 cases the motor and sensory portions were involved, and in the third only the sensory portion.

The abducens nerves were involved in 3 cases. Signs of increased intracanial pressure were lacking in 2 of the cases, and it was concluded that the disturbed function was due to direct involvement of the nerves or their nuclei by the neoplasm.

The facial nerves showed impaired function unilaterally in 4 cases. In 1 case facial paralysis was the first symptom noted.

The vestibular portion of the eighth cranial nerve was involved in 3 cases. In 3 other cases its function could not be tested, and in the seventh the tests were of doubtful value. The acoustic portion of this nerve was involved in only 2 instances.

The glossopharyngeal nerves were unilaterally impaired in 3 cases. In 3 other cases they were normal, and in the seventh their function could not be tested.

The function of the vagus nerves was lost or greatly impaired in 4 cases. In 3 of these cases the larynx was not observed, but the loss or impairment of speech led us to conclude that laryngeal paralysis was present.

The muscles supplied by the spinal accessory nerves were distinctly paretic in only 1 instance.

The hypoglossal nerves were involved in 3 cases. In 1 of these the musculature of the tongue was uniformly atrophied, although it could be protruded in the midline. In the other 2 cases only one half of the tongue was involved.

Progression of Symptoms.—The course of the illness in all instances was progressive, though often slowly so. Periods of months in which symptoms remained stationary were not uncommon. There was no remission of symptoms in any of our cases, though Brock and Needles in their report of a study of similar cases stated that remissions sometimes occur.

LOCALIZATION

Tumors originating in the pineal gland and cerebellum are probably most commonly confused with those of the stem. Horrax [5] studied and reported the differential points in localization of tumors primarily pineal

5. Horrax, G.: Differential Diagnosis of Tumors Primarily Pineal and Primarily Pontile, Arch. Neurol. & Psychiat. **17**:179 (Feb.) 1927.

from those primarily pontile in position. His study was based on 30 cases, in 15 of which the tumor was in the pineal gland, and in the other 15 of which it was in the pons. In his series all of the patients with pineal tumors first had symptoms of a general increase of intracranial pressure, while in those with pontile growths only 6 had similar symptoms at the onset of the illness. Hearing was impaired in 4 of the cases of pineal tumor and in several of the cases of pontile tumor. Sensory diminution over one half of the body was noted in 8 of the patients with pontile tumor and in only 1 with the lesion in the pineal gland. Papilledema was present in 60 per cent of the cases of pontile tumor and in 93 per cent of the cases of pineal tumor. Oculomotor disturbances were observed in 13 of each group. In 7 cases of pineal tumor, however, there was paralysis of upward gaze. This phenomenon was lacking in all of the cases of pontile tumor. Pupillary reaction to light was absent in 5 of the cases of pineal tumor, while in none of the cases of pontile tumor was such a disturbance of function noted. Disorders of the cranial nerves were much more commonly noted in the cases of pontile tumor; in fact, only occasionally was there a similar dysfunction in cases of pineal neoplasms. Hemiplegia was observed in 9 of the cases of pontile tumor and absent in all of the cases of pineal tumor. Pseudocerebellar signs were present in 11 of the cases of pineal tumor, and in all of the cases of pontile tumor.

In our series of cases, though we did not study the pinealomas, the symptoms, signs and manner of onset of the illness in the patients with tumors of the stem correspond with those observed by Horrax in his cases of pontile gliomas. A study of the clinical signs in our patients points to the localization of the tumor in the pons or medulla rather than in the pineal gland, if the differential factors pointed out by Horrax are used. Our personal observation of patients with pineal tumors likewise confirms these points of differentiation.

Tumors of the cerebellum in a few instances may be confused with those of the brain stem. The latter frequently first manifest themselves by cerebellar disturbances, and these symptoms may predominate in the clinical picture. On the other hand, cerebellar tumors may press on and invade the brain stem so as to produce disturbances of some of the cranial nerves. It is in these cases that an exploratory operation is frequently necessary to prove the correct localization. A complete history of the onset and progression of symptoms frequently aids in localizing the lesion.

The problem of clinically differentiating a neoplasm in the brain stem from one arising about the acoustic nerve is occasionally a difficult one. This is due partly to the fact that neoplasms in the brain stem may extend outward into the cerebellopontile angle and produce symptoms

similar to those caused by a perineurial fibroblastoma of the eighth nerve. On the other hand, tumors arising about the acoustic nerve may similarly extend medially to cause pressure on the brain stem. In our cases this problem of differentiation did not arise. The fact that our patients were all children, in whom tumors of the acoustic nerve are exceedingly rare, aided somewhat in eliminating this type of lesion. The development and progression of symptoms in our patients were entirely different from what is usually seen in acoustic new growths.

Horrax and Buckley reported a series of 25 cases of pontile glioma, in 8 of which an operation was performed for a suspected acoustic neoplasm; in all of the cases the tumor extended into the cerebellopontile angle. These investigators pointed out that a study of the chronological development of symptoms plays an important part in the diagnosis. Patients suffering from the effects of tumor of the acoustic nerve generally have a rather characteristic history concerning the onset of tinnitus followed by deafness, and possibly signs referable to the facial or trigeminal nerves. The onset of increased intracranial pressure usually follows these symptoms and is subjectively noted rather suddenly. On the other hand, one does not as a rule find a stereotyped history concerning symptoms produced by a tumor of the stem. The history of isolated conditions of cranial nerves or projection pathways of the stem with progression of symptoms should make one suspicious that a neoplasm may be present in the stem. Horrax and Buckley [6] have further pointed out that the sudden development of advanced papilledema and marked hydrocephalus is more apt to occur with tumors of the acoustic nerve than with tumors of the brain stem.

HISTOPATHOLOGY

The tumors of the brain stem described included 3 fibrillary astrocytomas, 3 multiform glioblastomas and 1 polar spongioblastoma. These differed in no essential respects histologically from similar tumors described elsewhere in the central nervous system.

In 3 of the cases the tumor was confined purely to the brain stem. In a fourth case it extended into the cervical cord, in another case into one cerebellar peduncle and in 2 others into the hypothalamic region. In all of these cases, however, the neoplasm was primarily one of the stem and appeared from gross and histologic evidence to have arisen there.

The 2 tumors about the aqueduct were small and of slow growth. Orton [4] pointed out that such lesions might produce no clinical symptoms

6. Horrax, G., and Buckley, R. G.: A Clinical Study of the Differentiation of Certain Pontile Tumors from Acoustic Tumors, Arch. Neurol. & Psychiat. **24**:1217 (Dec.) 1930.

if located elsewhere in the brain. They form a separate group among the gliomas of the stem, which are important by virtue of their position. In their paper on periaqueductal lesions, Sheldon, Parker and Kernohan [7] stressed the same point.

COMMENT

The problems concerning the localization and clinical diagnosis of gliomas arising in the brain stem have been discussed. It would be of advantage to the clinician if a definite syndrome could be established as characteristic of neoplasms in this location. From the reports published by others and a study of our own cases the establishment of such a syndrome presents considerable difficulty. This difficulty is obvious when one reviews the early history of patients with tumors of the brain stem. Frequently only one function of the cranial nerves is altered for some time, and it is during this period that so many errors in diagnosis are apt to occur. During the early part of the illness one is apt to consider a neoplasm as the least likely diagnosis.

One of the remarkable features in our group of cases was the age of incidence. In this small series, 6 of the patients were under 10 years of age, and 1 was 16. In the series reported by Brock and Needles, the only patient with an intramedullary glioma was 16. Three of the tumors in their group were extramedullary, and the patients were all adults. In the 25 cases reported by Buckley most of the patients were children. Of the 10 patients with glioblastomas, 7 were children, and of the 6 with fibrillary astrocytomas, 3 were under 14 years of age. The 2 patients with protoplasmic astrocytomas were adults.

The problem of surgical intervention in patients with suspected tumors of the stem offers at times considerable difficulty. This is particularly true in cases in which the localization is in doubt. In patients in whom the lesion is obviously intramedullary operation certainly is contraindicated. In most instances these patients withstand any form of operation poorly. In the 7 cases under consideration, 6 patients were operated on. One died two hours after the procedure, 2 lived for several days, 2 others for three or four weeks, and 1 for fourteen weeks after the first operation. Operative procedures in these cases consisted of exploration of the posterior cranial fossa or subtemporal decompression. In 1 instance the lateral ventricles were tapped, and death followed in a short time. On the other hand, it would appear more logical in our opinion to operate if there is any doubt as to the localization of the lesion. The benefits derived from the removal of a cerebellar or acoustic

7. Sheldon, W. D.; Parker, H. L., and Kernohan, J. W.: Occlusion of the Aqueduct of Sylvius, Arch. Neurol. & Psychiat. **23**:1183 (June) 1930.

tumor or the drainage of a cyst in most instances outweigh the shortening of the life of patients with a tumor of the stem, who at best are destined to live only a short time.

SUMMARY AND CONCLUSIONS

1. The clinical signs and autopsy findings in 7 cases of glioma of the brain stem are reported.

2. In 3 of the 7 cases the neoplasm was an astrocytoma fibrillare, in 3 a glioblastoma multiforme and in 1 a polar spongioblastoma. The histologic structure was similar to that found in the same types of tumors situated elsewhere in the brain.

3. The extent of the neoplasms as seen at autopsy was usually much greater than one would have suspected from a study of the clinical signs and the course of the disease.

4. Considerable difficulty may be encountered in establishing the clinical diagnosis in a case of tumor of the brain stem. A history taken carefully and completely with regard to the manner of onset of illness and the progression of symptoms is of great diagnostic aid.

5. If a diagnosis of tumor of the posterior fossa is established, and there are signs of a nuclear involvement of the cranial nerves, one should suspect that the lesion is completely or partially intramedullary.

6. The intramedullary gliomas are somewhat more frequent in children than in adults.

7. An exploratory operation of the posterior cranial fossa should be performed if there is doubt as to whether the tumor is inside or outside the brain stem. If the localization is obviously intramedullary, cranial operative procedure is contraindicated.

THE RUBROSPINAL TRACTS IN THE MONKEY

EFFECTS OF EXPERIMENTAL SECTION

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The several functions associated with the rubrospinal system can best be outlined under the headings: (1) functions as a conduction pathway from the cerebellum and (2) functions intrinsic in the red nuclei themselves.

REVIEW OF THE LITERATURE

Functions as a Conduction Pathway.—Cerebellar Muscular Incoordination: Clinicians and experimentalists are agreed that irregularity in muscular movement is the outstanding symptom to persist following extensive injury to the cerebellum. It is also agreed that incoordination is most obvious in voluntary movement. In fact, there is growing evidence [1] that cerebellar ataxia is solely a function of the voluntary system as exemplified in the following statement by Walshe [2]: "There is no such phenomenon as cerebellar ataxia in the reflex preparation. It is solely voluntary movement, therefore, which is dependent upon cerebellar activity."

That muscular incoordination might result from interruption of the rubrospinal path has been assumed largely on the basis of the well known outflow of fibers from the cerebellar nuclei over the superior cerebellar peduncles. It is unmistakable that clinical,[3] experimental [4] and anatomic [5] literature assumes that the coordinating rôle of the cerebellum is mediated over the superior peduncles.

The expenses of this investigation were aided by a grant from the Ella Sachs Plotz Foundation.

From the Department of Physiology and Pharmacology, University of Alabama School of Medicine.

Read in Section on Neurology and Psychiatry, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Va., Nov. 17, 1933.

1. (*a*) Fulton, J. F.; Liddell, E. G. T., and Rioch, D. McK.: Relation of Cerebrum to Cerebellum: Cerebellar Tremor in the Cat and Its Absence After Removal of the Cerebral Hemispheres, Arch. Neurol. & Psychiat. **28**:542 (Sept.) 1932. (*b*) Dusser de Barenne, J. D., quoted by Fulton, Liddell and Rioch.[1a] (*c*) Rademaker, G. G. J., and Winkler, C., quoted by Fulton, Liddell and Rioch.[1a]

2. Walshe, F. M. R.: The Significance of the Voluntary Element in the Genesis of Cerebellar Ataxy, Brain **50**:377, 1927.

(Footnotes continued on next page)

So far as we can determine, there has been no localized lesion reported clinically which was confined to the rubrospinal system or any experimental work on primates that would indicate directly that injury to the rubrospinal system results in muscular incoordination. Ferrier and Turner's [4] monkeys exhibited marked and characteristic irregularity in movement after section of the superior cerebellar peduncles. The disturbance was interpreted as being due to interruption of the cerebello-rubrospinal path.

Mussen's [6] cats, in which he destroyed the paleorubrospinal tracts bilaterally at their source, exhibited a syndrome of awkwardness of the limbs which disappeared rapidly. Whether or not dysfunction was permanent is not known since he killed his animals a few weeks after operation. Ingram and Ranson,[7] repeating Mussen's experiment, described in more definite terms awkwardness of the limbs following bilateral lesions which they seemingly ascribed to interruption in the cerebello-rubral path.[8] Their experiments were also based on essentially acute preparations.

By section of the rubrospinal tracts as they pass caudally through the lateral part of the pons we have been able in the cat and dog to section these tracts unilaterally without so much as transitory signs of any type of dysfunction. However, a homolateral syndrome, characterized by a loss of placing of the limbs with a resultant awkwardness in position of the limbs, has been encountered when a lesion encroaches on the medial quarter segment (fig. 1) at the level of the pons or caudal portion of the midbrain. Medial longitudinal section through the caudal midbrain produces the syndrome bilaterally. Immediately following a lesion there is in the limbs a gross awkwardness of position with frequent use of the dorsa of the feet and the ankles in standing and

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3. (*a*) Hunt, J. Ramsey: Dyssynergia Cerebellaris Myoclonica; Primary Atrophy of the Dentate System: Contribution to Pathology and Symptomatology of Cerebellum, Brain **44**:490, 1922. (*b*) Bailey, P.: Intracranial Tumors, Springfield, Ill., Charles C. Thomas, Publisher, 1933. (*c*) Holmes, Gordon: The Symptoms of Acute Cerebellar Injuries Due to Gunshot Injuries, Brain **40**:461, 1917.

4. Ferrier, D., and Turner, A. W.: Phil. Tr. Roy. Soc. London **185**:719, 1894.

5. Bailey.[3b] Papez, J. W.: Comparative Neurology: A Manual and Text for the Study of the Nervous System in Vertebrates, New York, Thomas Y. Crowell Company, 1929.

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7. Ingram, W. R., and Ranson, S. W.: The Place of the Red Nuclei in the Postural Complex, Am. J. Physiol. **102**:466, 1932; Effects of Lesion in the Red Nuclei in Cats, Arch. Neurol. & Psychiat. **28**:483 (Sept.) 1932.

8. Ingram, W. R., and Ranson, S. W.: Postural Reactions in Cats Following Destruction of Both Red Nuclei, Proc. Soc. Exper. Biol. & Med. **29**:1089, 1932.

walking, and also some awkwardness in the movements of progression. The impairment decreases and changes somewhat in form following operation but eventually remains stationary. In our first work,[9] accordingly, we interpreted the impairment noted as being due to section of the rubrospinal tract or of ascending afferent tracts. We are not as yet certain, however, whether this syndrome in the cat and dog is precipitated by section of a brachium conjunctivum or that of structures in the medial quarter segment. In our lesions the brachium conjunctivum was completely sectioned only when the medial quarter segment had been involved.

Spontaneous Static Tremor: Gordon Holmes[10] described several variations of static tremor in cerebellar disease, all of which are precipitated by some sort of strained posture. Since they are associated with posture they can be explained on the same basis as muscular incoordination, that is, asynergia, asthenia or atonia, and necessarily cannot be called spontaneous. Regarding a rare type of static tremor seen in man, Holmes said:

> A similar regular tremor occurs more rarely in portions of the body which are not fully supported. Its resemblance to the tremor of paralysis agitans is unmistakable; it is apparently similar to that which Ferrier and Turner observed after section of the superior peduncles, and which is frequently associated with midbrain lesions that involve these peduncles. In my only two cases of gunshot wounds in which it was a prominent feature, the course or position of the missiles made it probable that the superior peduncles were injured. It occurred also in a man lately under my observation in whom an extensive tumor was found by operation to extend towards the anterior margin of the cerebellum, where it probably involved one superior peduncle.

Ferrier and Turner[4] described clearly a spontaneous tremor in the monkey which made its appearance several days following operation, ultimately disappearing after several weeks. This tremor occurred homolaterally and involved either the forelimb or both limbs simultaneously. It appeared at times to become more intense with excitement, and although it was observed when posture was strained it was present when the animals were at complete ease. The tremor occurred in animals in which the superior peduncles had been sectioned as well as in animals with other cerebellar injuries.

So far as we can determine there is no direct evidence that section of a rubrospinal tract results in the release of a spontaneous static

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9. Keller, A. D., and Hare, W. K.: Localization of the Mechanisms for Righting in the Brain Stem of the Cat, Proc. Soc. Exper. Biol. & Med. **30**:190, 1932; The Independence of the Righting Reflexes and of Normal Muscle Tone From the Rubrospinal Tracts, Am. J. Physiol. **105**:61, 1933.

10. Holmes, Gordon: Clinical Symptoms of Cerebellar Disease, Lancet **1**: 1177, 1922.

tremor. It is true that the tremor and the choreo-athetoid movements that occur in Benedikt's syndrome have been attributed to destruction of a red nucleus. However, we are familiar with no case in which the pathologic change was confined solely to the rubrospinal system.

Intrinsic Functions of the Red Nuclei.[11]—Spontaneous Involuntary Movements: In the literature the rubrospinal system has likewise been suggested repeatedly as being the extrapyramidal structures mediating spontaneous involuntary movements. Strong,[12] quoting Walshe, stated that following lesions of the superior peduncles involuntary movements appeared which were choreiform or choreo-athetoid rather than the voluntary ataxic movements seen after cerebellar injury. Wilson [13] has explained tremor, as seen clinically, as due to a release of extrapyramidal systems from higher control.

Inhibition of Extensor Tonus: Increased extensor tone in acute preparations has been repeatedly described as resulting from transection of the brain stem through the caudal level of the midbrain by removal of the tissue ahead of the transection. Rademaker [14] concluded from his work that the red nuclei were responsible for inhibition of extensor tonus, thereby maintaining a normal distribution of muscle tone in an intact or thalamic animal. Mussen's [6] experiment demonstrated definitely that the red nuclei were not essential for the apparently normal distribution of postural tone in an otherwise intact animal. Ingram and Ranson,[7] in the light of experience in repeating Mussen's experiment, believed that the red nuclei do play a definite though minor rôle in the inhibition of extensor tonus.

We have been unable to demonstrate any increased extensor tonus in cats and dogs with the rubrospinal tracts cut unilaterally or bilaterally.[9] This has also been our experience, except in a few instances in which the lesion has been unduly traumatic, in acute, subacute and chronic preparations of the midbrain and pons.[15] Pontile animals prepared by our method [15] presented no resistance to passive flexion; they retained

11. By this term we do not wish to imply that impulses are supposed to be discharged from the red nuclei in the absence of incoming impulses, but rather that the impulses mediating righting or tonic reflexes are changed from the afferent to the efferent limb of the arc in these nuclei.

12. Strong, O. S.: Unsolved Problems Suggested by Cerebellar Connections and Cerebellar Histology, Arch. Neurol. & Psychiat. **19**:1 (Jan.) 1928.

13. Wilson, S. A. K.: Disorders of Motility and of Muscle Tone with Special Reference to the Corpus Striatum, Lancet **2**:268, 1925.

14. Rademaker, G. G. J.: Die Bedeutung der roten Kerne und des übriges Mittelhirns für Muskeltonus, Körperstellung und Labyrinthreflexe: Monographien aus dem gesamtgebiete der Neurologie und Psychiatrie, Berlin, Julius Springer, 1926.

15. Keller, A. D.: Autonomic Discharges Elicited by Physiologic Stimuli in Midbrain Preparations, Am. J. Physiol. **100**:576, 1932.

tonic neck reflexes and exhibited reflex standing. They were unable to maintain the standing position owing, no doubt, to partial destruction of the righting mechanisms.

Righting Reflexes: Rademaker,[14] by placing lesions in the red nuclei and cutting the rubrospinal tracts as they cross the midline, concluded that the rubrospinal system is essential for (1) the labyrinth righting and (2) the body-righting reflexes acting on the body. Although Mussen[6] and Ingram and Ranson[7] studied righting reflexes superficially, they demonstrated clearly that the paleorubrospinal systems were not essential for an animal to right to its feet from the side or back and to progress without falling.

Our experiments on the localization of the central righting mechanisms have convinced us that conclusions cannot be drawn from acute preparations when they exhibit impairment of function, and our chronic preparations were not sufficiently numerous to allow a comprehensive report. Our experiments have, however, demonstrated that:

1. An acute or chronic midbrain cat (section of the anterior end of the superior colliculus dorsally and of the caudal end of the mamillary body ventrally) maintains the ability to right to its feet and progress without falling and to right in falling through the air. Such a cat maintained the righted position continually even to the point of the development of a necrosis from pressure involving the pads of the feet.

2. A pontile cat or dog possesses the essential mechanism for reflex standing, when propped, and the necessary pattern for progression.

3. Acute or chronic preparations in which the rubrospinal tract has been cut on one or both sides—the lateral quarter segments (monkey 12)—exhibit no alteration or asymmetry in any of the righting reactions. This is true also when the corticospinal system is subsequently removed.

OBSERVATIONS ON MONKEYS

Since voluntary movement is much more highly developed in the monkey than in the cat or dog, particularly movements that are truly voluntary in origin, the investigation of the function of the rubrospinal system in this species seemed highly desirable.

METHODS

Operative Procedure.—Under anesthesia with pentobarbital sodium, the dorsal surface of the midbrain was exposed by turning down a large flap of bone and exposing the dorsal and lateral aspects of the caudal two thirds of the cerebral hemisphere. The occipital pole was then retracted laterally, thus exposing with excellent visibility the dorsal aspect of the cerebellar tentorium, the corpora quadrigemina and the caudal aspect of the corpus callosum. The operative procedure in making this exposure was bloodless. The lesions were placed by our method[15] of blunt dissection. A no. 8 milliner's needle, firmly fixed in a needle

holder, was projected ventrad—with the blunt end forward—in what was judged to be the desired direction until the base of the skull was reached. It was then pulled gently laterad through the tissue of the brain until the peripheral bone was reached. This allowed complete section of fibers passing at an angle to the path of the needle, and left a minimum of blood and edema in and adjacent to the lesion, as evidenced by histologic studies as well as by the postoperative reactions of the animals. The blunt end of the needle made possible complete sections at the periphery of the stem without cutting vessels at the surface, as shown in the figures.

Preparation of Tissues.—At the termination of the experiment the brains were given an injection of a warm saline solution, followed by a 10 per cent solution of formaldehyde U.S.P. The complete brain stems were sectioned serially, every third or fourth section being stained for fiber tracts by a modified Pal-Weigert method worked out by one of us [16] (W. K. H.). The method also makes it possible to stain an adjacent series of sections for cells. This allows for an accurate localization of the lesion, and a careful study of chronic lesions in the tissues for (1) the presence or absence of groups of cells and (2) degenerated bundles of fibers.

Description of Lesions.—To facilitate description of lesions we have considered a cross-section of the brain stem as a circle and have divided it into segments. This is represented in the diagram of a circle divided into four segments which is drawn over a section showing the lesion in monkey 10 (fig. 1). Here the lesion involved completely the lateral quarter segment on the left and encroached slightly on the medial quarter segment dorsally.

Criterion for Successful Section of a Rubrospinal Tract.—Our criterion at the outset for successful section of a rubrospinal tract was the retrograde degeneration of the cells in the opposite red nucleus. That such retrograde degeneration resulted in the large cell (magnocellular) or caudal red nucleus following section of a lateral quarter segment of the brain stem in the pons is demonstrated in figures 1 and 2. It will be noted, however, that retrograde degeneration of cells did not occur in the opposite small cell (microcellular) red nucleus but did in the homolateral nucleus.

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16. The tissue fixed in formaldehyde is blocked and washed overnight in running water, then mordanted according to the method of Weigert: It is (*a*) placed for from four to seven days in a solution of fluorchrome, 5 Gm. of potassium dichromate, 2 Gm. of chromium fluoride and 100 cc. of distilled water, (*b*) washed overnight in running water and (*c*) placed for from two to four days in a solution of 5 Gm. of copper acetate, 2 Gm. of chromium fluoride, 4 cc. of acetic acid and distilled water to make 100 cc. The tissue is then embedded in pyroxylin (celloidin) and cut at from 40 to 60 microns and the sections kept in serial order. The sections are treated for from two to three minutes in a 0.5 per cent solution of potassium permanganate and transferred to a saturated solution of sodium sulphite to which a few drops of acetic acid have been added. When completely decolorized they are washed thoroughly and mordanted for thirty minutes in Benda's iron mordant, diluted with four parts of 95 per cent alcohol to one part of the mordant. After a thorough washing the sections are stained from two to three hours (or until blue-black) in a 1 per cent solution of hematoxylin in 70 per cent alcohol. The sections are differentiated by treating them with a 0.1 per cent solution of potassium permanganate until the gray matter is brown. They are decolorized in the solution of sodium sulphite. If differentiation is insufficient it is completed in Benda's iron mordant. Sections may be washed and counterstained for cells with neutral red after the method of Kirkman (Anat. Rec. **51**:323, 1932).

Fig. 1.—Cross-section of the pons in monkey 10 over which a circle, divided into four segments, has been drawn, thus dividing it into right and left medial and lateral quarter segments. The lesion involves all of the left lateral quarter segment and part of the left medial quarter segment.

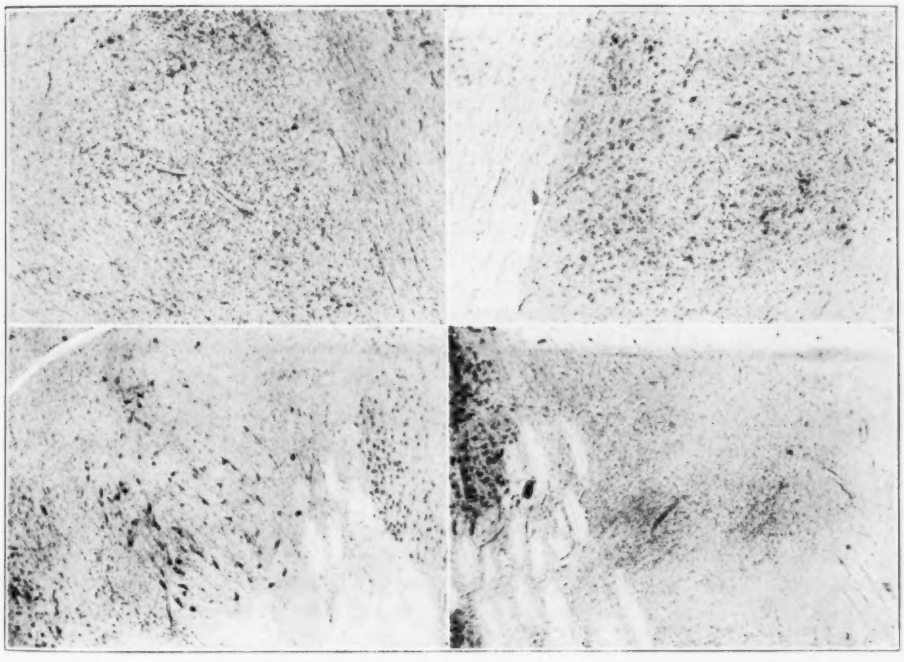

Fig. 2.—Lower Quadrants: Photomicrographs of portions of the right and left large cell red nuclei following section of the lateral quarter segment of the pons or lower midbrain shown in figure 1. The contralateral, large cell red nucleus shows retrograde degeneration; the homolateral, none. Upper Quadrants: Portions of the right and left small cell red nuclei in the same animal, showing degeneration in the homolateral nucleus but none in the contralateral.

RESULTS

Our colony consisted of thirteen animals. Monkeys 1 and 13 died of miliary tuberculosis before operation. In monkey 3 the brain stem was hemisected at the middle level of the midbrain in connection with another problem. Another, monkey 4, died on the operating table from respiratory failure as a result of the needle reaching caudally into the region of the obex. Several days after pontile lesions were placed, monkeys 2, 5 and 11 died with diarrhea and bleeding of the bowel. The remaining six monkeys were maintained to the chronic and prechronic states after pontile lesions were placed.

Muscular Incoordination.—This was encountered in varying degrees in the homolateral limbs following seven of the nine successful lesions. The incoordination was characterized by: (1) Overreaching or groping for food in a clumsy manner, each attempt being a more or less isolated movement. After the hand succeeded in grasping the food it was moved rapidly in an apparently normal manner toward the mouth, where again overreaching often occurred, the mouth being missed and the nose, eye or cheek being struck instead. (2) A tremor of the arm, more noticeable in the hand, which appeared as the hand approached the mouth and while the food was held at the mouth. This intention tremor varied from fine, barely noticeable oscillations to coarse ones which in one animal simulated closely the isolated clumsy overreaching movements. In mild cases the tremor usually consisted in only one or two oscillations and appeared only occasionally, for at other times food was placed to the mouth with no evidence of dysfunction. (3) In the more marked cases lifting of the ipsilateral limbs higher from the floor in walking than the contralateral limbs, planting them on the floor with definitely added force. This planting of the affected limbs on the floor was readily audible at a distance. The animals which exhibited "slapstick ataxia" in walking also staggered to the affected side during the acute and subacute stages, the staggering gradually disappearing as the preparation became chronic. These animals also held the forelimb across the chest, more or less constantly, in a hemiplegic posture. Also the unaffected limb was used when possible in preference to the involved limb.

A summary of the results obtained in the experiments is charted in table 1. It is to be noted from table 1 that following the placing of the left lesions in monkeys 7 and 12 muscular incoordination was present but was of short duration; it was completely absent following placing of the right lesion in monkey 12.

Monkey 7 exhibited a slight overreaching and intention tremor in feeding for a few days after operation. This disturbance disappeared rapidly and completely. On the ninth day the arm was used freely, with no dysfunction. The lesion involved approximately the lateral quarter segment at the middle of the pons.

On the day following the placing of the left lesion, monkey 12 (fig. 3) exhibited a rather marked ataxia in the left arm in reaching for food but displayed no

ataxia or intention tremor in placing food to the mouth. This dysfunction disappeared rapidly, there being no trace of disturbance in movement on the seventh day. The lesion involved the lateral quarter segment in the cephalic portion of the pons.

On the first day following the placing of the right lesion (fig. 3) in monkey 12 there was no evidence of disturbance in feeding movements. Impairment of function was manifested, however, by an awkwardness in holding food in the hand

TABLE 1.—*Correlation Between the Structures Involved by the Lesions and the Amount and Duration of Muscular Incoordination and Tremor in the Corresponding Arm*

			Degree of Involvement of Cerebellar Structures by Lesion					
Monkey with Left Lesions	Left Arm		Rubrospinal Tract	Brachium Conjunctivum	Brachium Pontis	Ventral spinocerebellar Tract	Hook Bundle	Vestibular Nuclei
	Attack	Tremor						
6	+ Permanent	Postural + Temporary	Complete	Complete	¼ ±	Complete	Possible trace	0
7	+ Temporary	0	Complete	¾ ±	⅓ ±	Suspected	0	0
8	++ Temporary	Spontaneous + Temporary	Complete	Complete	⅓ ±	Complete	Some	Trace ?
9	+++ Temporary (?)	Spontaneous ++ Temporary	Complete	0	0	Complete	0	Some
10	++++ Permanent (?)	Spontaneous ++++ Permanent (?)	Complete	Complete	¾ ±	Complete	Trace ?	
12	+ Temporary	0	Complete	½ ±	¼ ±	0	0	0
With Right Lesions	Right Arm							
12	0	0	Complete	⅓ ±	¼ ±	0	0	0
8	0	0	0	0	0	0	0	0 ?
7	++ Temporary	0	¾ ±	¾ ±	0	Complete	Some	Some

and by a hesitancy in assuming the upright position, either while at rest or during progression. Also in walking the limbs were widely placed and the fore quarters were carried slightly higher than the hind quarters. This awkwardness disappeared completely, though slowly, over a period of from three to four weeks. The following is taken from the protocol in the case of monkey 12:

First Day After Right Lesion: Forenoon: Picked up banana immediately with left hand and placed it to mouth without any disturbance. When left hand was held, picked up banana with right hand and placed it to mouth without any noticeable ataxia or tremor; however, held banana in hand rather awkwardly and dropped it while feeding, as though grasp was weak. On a second attempt held banana with wrist flexed. 5:30 p. m.: Monkey rested on dorsum of right hindlimb (similar to dogs and cats).

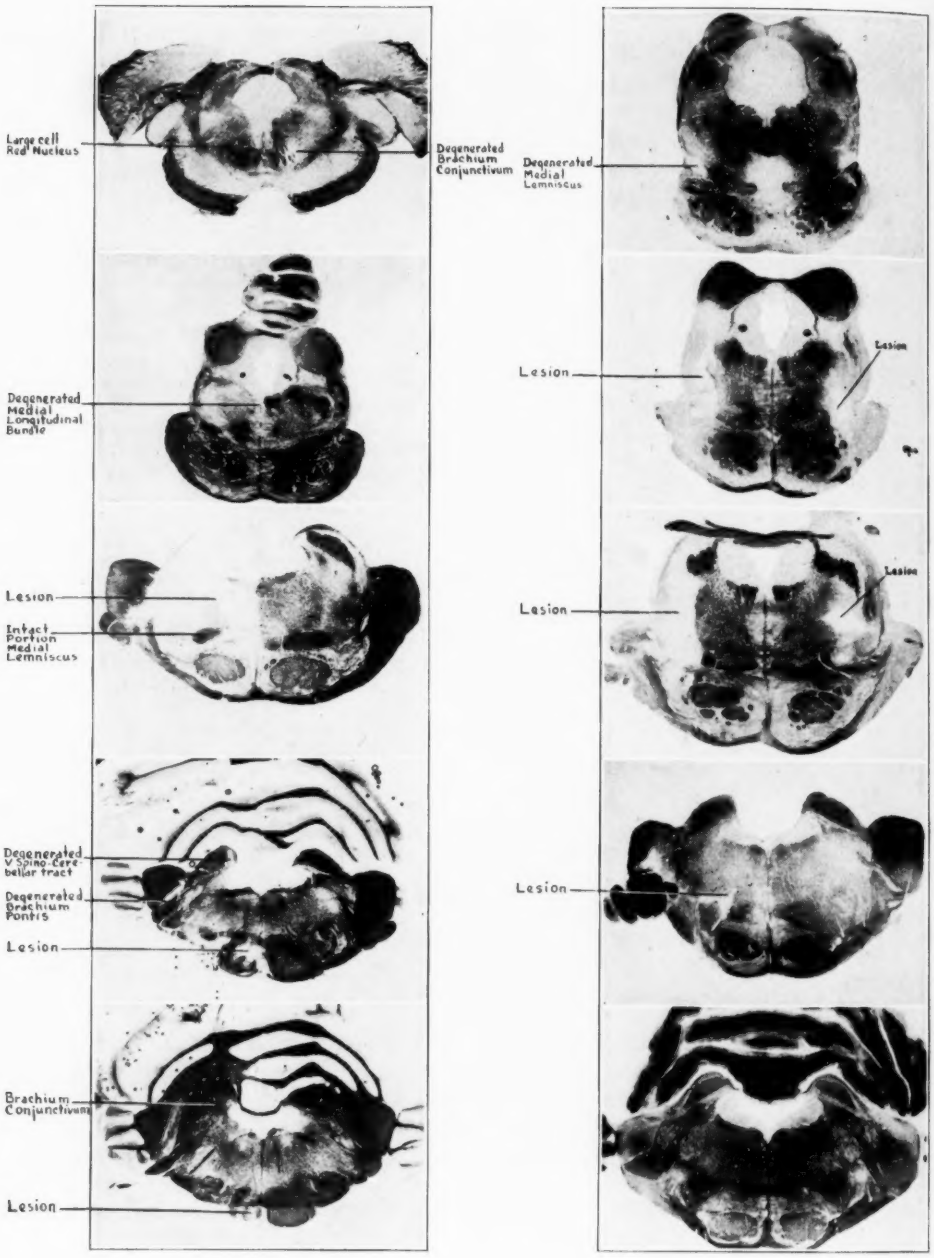

Fig. 3.—Photomicrographs of sections taken from the brain stems of monkeys 6 and 12, demonstrating: (1) the location and extent of the lesions and (2) degenerated fiber bundles.

Second Day After Right Lesion: Monkey very alert, maintaining righted position at all times and sitting on haunches. However, had difficulty in keeping hindlimbs flexed for this position, in that they seemed to slip out along the floor very easily. Yesterday monkey used left arm in feeding with distinct preference

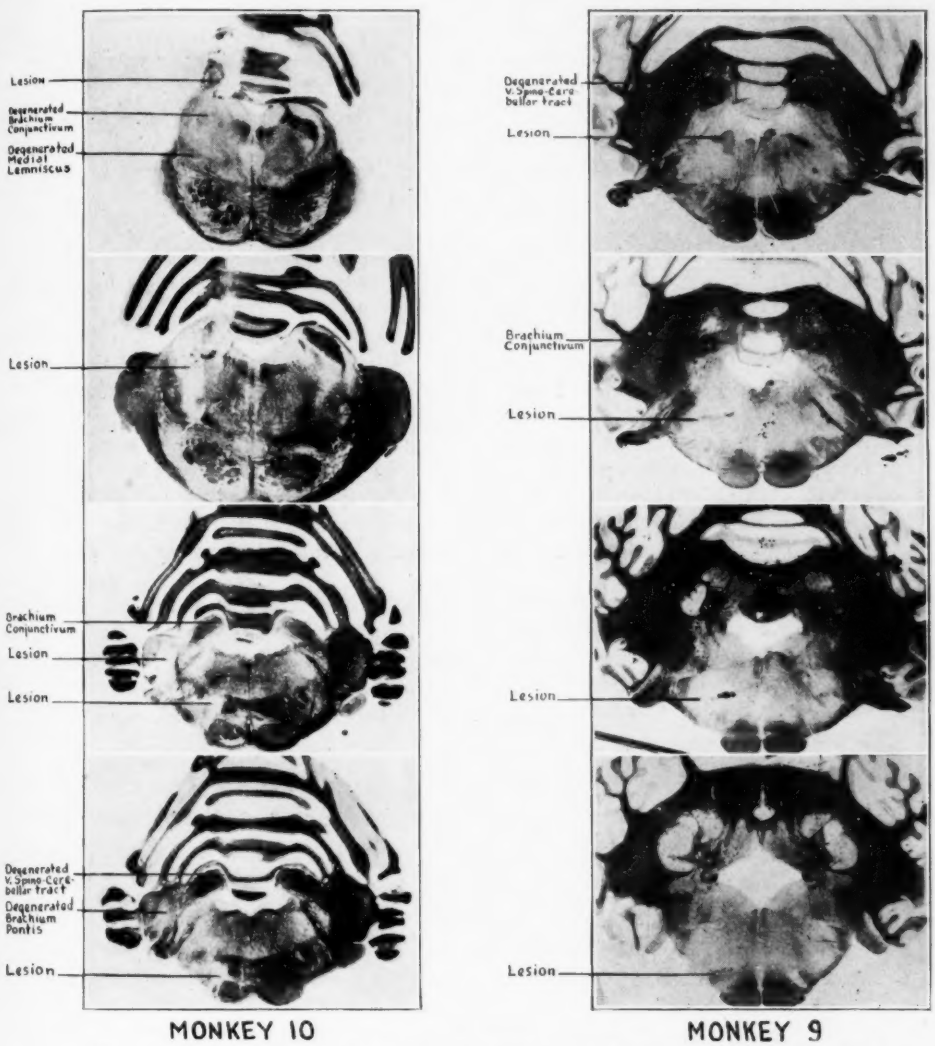

Fig. 4.—Photomicrograph of sections taken from the brain stems of monkeys 9 and 10, demonstrating: (1) the location and extent of the lesions and (2) degenerated fiber bundles.

to the right. Today this preference was reversed; reached for food readily with right arm and placed it to mouth without ataxia or tremor. Occasionally when banana was some distance away made several attempts before getting it in hand but not by clumsy overreaching movements.

Sixteenth Day After Right Lesion: Excellent physical condition; wild; almost back to preoperative level. Walked on all fours in upright position very readily. Had tendency, however, to walk with hind quarters slightly flexed so that they were carried lower than fore quarters. Although walking was somewhat awkward, there was no tendency to lose balance. In running, he had a tendency to leap like a rabbit. Picked up small individual grains of rice with right hand and placed them to mouth without slightest disturbance in movement.

One Hundred and Eighteenth Day After Right Lesion: Monkey in excellent condition. Showed absolutely normal movements during any act.

In another group (left lesion in monkey 8 and right lesion in monkey 7) muscular incoordination was present in a somewhat more marked degree immediately after operation and persisted over a longer period of time than in the previous group. The disturbance in movement disappeared gradually, and complete recovery was attained.

In monkey 6 following operation a slight ataxia and intention tremor involved the left arm and persisted until death, eight and one-half months after the lesion was placed. The arm at times executed feeding movements with no apparent disturbance. The symptoms following operation were only slightly more marked than they were in the chronic state. The lesion essentially hemisected the brain stem.

Monkey 9 (fig. 4) displayed overreaching and intention tremor in a definitely more marked degree, and they persisted longer than in any of the previously mentioned monkeys. Whether or not dysfunction was still present at the time of death, seventy days after operation, was not certain because of the monkey's refusal to feed when under observation. This monkey displayed shyness before operation. However, the monkey carried the left arm in a semiflexed position across the chest up to the time of death, which indicated that some dysfunction was still present.

The most marked disturbance in movement encountered was in monkey 10 (figs. 1, 2 and 4). Although overreaching, intention tremor and "slap-stick ataxia" lessened considerably during the postoperative course, all the symptoms were clearly present just previous to the monkey's death, ninety-five days after operation. The left arm was continually held across the chest in a typical hemiplegic posture.

Static Tremor.—This was of two distinct types; one was elicited because of strained posture, the other was apparently spontaneous. (1) Postural tremor, as it was seen, involved the arm when holding food in a static position, that is, while holding a banana in the hand during the process of chewing a mouthful previously taken from it. The tremor was not constantly present but broke through at intervals. It was observed only in monkeys 2 and 6. The lesion in monkey 2 involved the lateral quarter segment in the middle portion of the pons. (2) Spontaneous tremor occurred in the homolateral limbs and made its appearance some days after operation and disappeared after several weeks. It was not present constantly but broke through at intervals. It was characterized by excursions varying from fine to coarse oscillations. Although it usually appeared when posture was not strained, it was accentuated in certain instances by movement and excitement. In monkey 10 a tremor was repeatedly seen to break through and involve the left forelimb simultaneously with the use of the right arm

in feeding movements. Spontaneous tremor was encountered only in monkeys 8, 9 and 10, being most marked in frequency of appearance and in duration in monkey 10 and somewhat less marked in monkey 9. It was seen only infrequently during a short period following the left lesion in monkey 8. It would seem significant that this tremor appeared in the animal exhibiting the most pronounced muscular incoordination.

The rubrospinal tracts were sectioned by all the foregoing lesions except the right in monkeys 7 and 8. In the right lesion in monkey 7, approximately three fourths of the large cells degenerated. There was no apparent degeneration in the cells of the left red nucleus in monkey 8.

The brachium conjunctivum was completely sectioned by the left lesions in monkeys 6, 8 and 10, and was involved in varying degrees in the other instances. It is to be noted from the photographs of the lesions in the cases of monkeys 6 and 10 (figs. 3 and 4) that, in the instance of the section of a brachium conjunctivum, complete degeneration occurred distal to, but not proximal to, the lesion; in the latter case the bundle showed only a slight thinning. Nissl preparations in each instance demonstrated intact cerebellar nuclei, except in that of the cephalic portion of nucleus emboliformis which was devoid of cells.

Righting Reflexes.—Righting reactions are as clearcut in the monkey as in the cat. However, care must be taken in ruling out the cerebral element, for a monkey may decide at any time to take the "attitude of a martyr" and inhibit all responses. A monkey rights rapidly in falling through the air, rights directly from the side by a rolling, lifting movement in which the arms as prehensile organs do not participate to any great extent. If the animal were passively rotated when standing on all fours by gripping the back in the lumbar region, the rotation would be compensated for by an active rotation of the head and fore quarters to the opposite side.

The left lesions in monkeys 7, 8, 10 and 12 and the right lesion in monkey 12 involved essentially only a lateral quarter segment. In all these instances righting remained symmetrical.

On the second day following operation, monkey 7 quickly righted directly from both sides with the eyes covered and turned equally well to either side while falling through the air.

Monkey 8 readily righted directly from both the right and left sides on the first day after operation. Righting in falling through the air was not tested until the eighty-second day. (The tests for righting in falling through the air were discontinued directly following operation, after it was learned that in the cat this procedure often elicited fresh hemorrhage about the lesion.) At this time the monkey turned equally well to each side in righting in the air.

Monkey 10 on the first day after operation righted from both sides, but this was slightly asymmetrical in that there was a tendency to indirect righting.[17] from the right side. On the eighth day the indirect tendency was not present. Clearcut reactions were never obtained from this monkey in falling through the air.

17. In indirect righting, the animal presses the head against the floor, extends the uppermost arm forward and toward the opposite side in a grasping attitude, and draws the undermost arm beneath the body.

On the third day after the left lesion was placed, monkey 12 righted indirectly from the right side; at this time the right limbs were paralyzed. On the twenty-seventh day there was no asymmetry in righting either from the sides or in the air. The following is from the protocol in the case of monkey 12:

First Day After Right (Second) Lesion: Direct righting from left side was brisk; very rapid from right side. Monkey up in righted position, sitting on its haunches. Resisted rolling to both sides markedly.

Eleventh Day After Second Operation: Righted rapidly directly from both sides, also righted body from both sides when the head was fixed laterally. In falling through the air, dorsum down, turned to left and also to right.

Fifty-Second Day After Second Operation: In falling through the air, absolutely no asymmetry; turned rapidly to either side in falling a short distance with the dorsum down at the start.

Monkey 6 following operation exhibited asymmetrical righting, by righting indirectly from the right side during the acute and subacute stages. There was a definite tendency to indirect righting from this side in the chronic state. In falling through the air he retained throughout a distinct preference to turn to the right side. The lesion in this instance was a hemisection, which involved the left medial quarter segment (fig. 3).

Following the right lesion monkey 8 in the chronic state exhibited a slight tendency to indirect righting from the left side. The picture in this case was complicated, however, by a permanent slight paralysis of the left limbs. The lesion involved most of the right medial quarter segment and left the lateral quarter segment intact.

Monkey 9 in the acute and subacute stages hyperactively righted directly from the left side and distinctly indirectly from the right side. In the chronic state hyperactive righting from the left side persisted, as did a tendency to indirect righting from the right side. In falling through the air there was a preference to turn to the left side. The lesion sectioned the lateral quarter segment, infringed on the medial quarter segment and reached slightly into the medulla caudally (fig. 4).

The lesion in monkey 5 involved both medial quarter segments of the brain stem at the level of the junction of the pons and medulla, leaving the lateral quarter segments intact. It reached slightly more laterally on the left side than on the right. The path of the lesion was filled by a thick clot of blood. The monkey exhibited a constant picture of decerebrate rigidity, with complete absence of any attempts at righting. The monkey was found dead on the morning of the sixth day after operation. The following is taken from the protocol:

November 7 (Fifth Day After Lesion) 9:00 a. m.: Monkey passed liquid bloody feces, and also some soft feces diffusely filled with blood. Appeared to be in good physical condition. Showed no attempt at righting or resistance to rolling, and did not attempt in any manner to maintain the righted position. Exhibited good reflex standing; tonic neck reflexes were easily demonstrated. He executed walking movements readily when held on all fours in the walking position. Vocalized in some degree spontaneously and freely when manipulated.

COMMENT

Physiologic Considerations.—Muscular Incoordination and Tremor: The disturbances in muscular movement and the spontaneous tremor seen in our experiments were undoubtedly of the same nature as those

seen by Ferrier and Turner [4] in monkeys following extirpation of a lateral lobe or vermis or after section of the superior or middle peduncle. The following description from the protocol of their experiment 4 is typical.

> After operation (removal of left lateral lobe) its motor power was good, because it was able to climb with ease and with a normal use of all four limbs.
>
> On the third day motor power was as before. It exhibited, on volitional effort with the left hand, wild and irregular movements.
>
> At the end of a week the animal sat at rest and undisturbed with its back in a corner and the left limbs adducted and flexed. There was observed, apart from obvious muscular exertion, a fine tremor of the head, upper part of the body, and of the left arm. These tremors passed on volitional effort, such as eating food, into irregular oscillations of considerable amplitude.
>
> At the end of a fortnight the gait was still unsteady and sprawling. The fine tremors in the arm and head were now more marked and were visible also in the left leg. There was no apparent difference in the muscle tone of the two sides.
>
> At the end of the fourth month when at rest the left limbs were adducted and flexed. In progression there was a somewhat sprawling action of the left arm and leg; they were raised and planted in an ataxic manner. When at rest there was no tremor, but irregular oscillations appeared on volitional effort as grasping for food.

It should be noted that the fine tremor which involved the head and left arm when at rest did not appear until several days after operation and eventually disappeared completely, whereas, "irregular oscillations in volitional effort, the raising and planting of the limbs in an ataxic manner in progression, and the adducted and flexed position of the limbs at rest," all remained and were constant four months after operation.

Our experiments differ from those of Ferrier and Turner in that the muscular incoordination present after operation was in most instances transitory. In monkey 6 incoordination was permanent, but it was slight in each of the acute, subacute and chronic states. Whether or not permanent dysfunction would have remained in monkeys 9 and 10 is problematic. The degree and duration of impairment was certainly more marked in these monkeys than in the others.

It can be seen from table 1 that the degree and duration of muscular incoordination and static tremor present after operation cannot be correlated with section of the rubrospinal tracts. The left lesion in monkey 7, the left lesion in monkey 12 and particularly the right lesion in monkey 12 demonstrate conclusively that the rubrospinal systems are not essential to normal muscular coordination in movement or the stability of muscle during rest, for example, so far as incoordination can be determined by observation. In the first two instances, although dysfunction was present directly following operation, it disappeared completely in a few days. Following the right lesion in monkey 12 there

was no irregularity in fine voluntary movements such as are necessary for picking up individual grains of uncooked rice and placing them to the mouth. Static tremor did not follow any of these lesions. In every instance serial sections of the midbrain demonstrated complete absence of the cells in the opposite large cell red nucleus and absence of the majority of the cells in the ipsilateral small cell red nucleus.

It is not clear whether the temporary awkwardness in holding food and the hesitancy in assuming the upright position in progression encountered in monkey 12 were the result of the bilateral absence of the rubral systems or of section or temporary dysfunction of other structures. For the solution of this question a larger series of animals will be necessary.

It is evident that the superior arm of the cerebellum is not essential for normal coordinated muscular movement and for the static stability of muscle. It will be noted from table 1 that the brachium conjunctivum was completely sectioned in only three instances, namely, in the left lesions in monkeys 6, 8 and 10. In monkey 8 the incoordination was moderate in degree and duration and completely disappeared. Although monkey 6 exhibited a slight incoordination that was permanent, it was relatively no more pronounced immediately after the operation than it was eight months later. The incoordination seen in monkey 10 approached that described in previous experiments in extirpation of the cerebellum and accordingly that which would be expected on section of the superior arm if coordination was dependent on the integrity of this peduncle. On the other hand, incoordination was marked in monkey 9 in which the superior cerebellar arm remained intact anatomically.

In the light of these observations it can be stated that if the coordinating function of the cerebellum is mediated from its lateral lobes there must be an outflow from the lateral group of nuclei other than that over the brachium conjunctivum. That such an outflow is possible has been emphasized by several authors, particularly by Strong.[12] If, however, the lateral lobes discharge only over their superior arms, as the work of Mussen indicates, then we are forced to the conclusion that they are not essential for coordinated voluntary movement.

One naturally wonders, therefore, if coordinated muscular movement is dependent on the brachium pontis. None of our lesions completely sectioned this peduncle. It was involved to some extent by the left lesions in monkeys 6, 7, 8 and 12, and by the right lesion in monkey 12. In monkey 10, in which dysfunction was most marked, it was almost completely sectioned; yet the brachium pontis was not involved anatomically by the lesion in monkey 9 in which incoordination and tremor were marked.

Careful analysis of table 1 shows that the incoordination and tremor encountered in our experiments cannot be correlated with destruction

of any known anatomic structure. The fact that a mechanism may be rendered temporarily nonfunctional, probably owing to adjacent hemorrhage and edema, without actual anatomic destruction is clearly illustrated in table 2, in which the degree and duration of paralysis are compared with the degree of involvement of the corresponding corticospinal tract.

It is readily seen that the amount and duration of paralysis were not proportional to the amount of involvement of the corticospinal tract. The paralysis in monkey 9, in which about a third of the tract was severed, was as great if not greater than that in monkey 6 in which three fourths of the tract was destroyed. There was no paralysis following the left lesion in monkeys 7 and 8 in which the tracts were

TABLE 2.—*Comparison of the Degree and Duration of Paralysis with the Extent of Involvement of the Corresponding Cerebrospinal Tract*

Monkey	Right Arm Paralysis	Degree of Involvement of Tracts by Lesion	
		Cerebrospinal Tract	Medial Lemniscus
With Left Lesions			
6	++ Temporary	¾ +	½ ±
7	0	¼ ±	⅓ ±
8	0	⅓ ±	⅓ ±
9	++ Temporary	⅓ ±	0
10	0	⅓ +	0
12	+ Temporary	Trace	¾ +
	Left Arm Paralysis		
With Right Lesions			
12	0	Trace	¾ +
8	+ Permanent	¾ +	Complete
7	+ Temporary	0	Trace

partially sectioned, yet there was complete temporary paralysis after the left lesion in monkey 12 in which the tract was barely touched.

When spontaneous tremor was observed it did not appear until a few days after operation, progressively became more intense and then entirely disappeared after the lapse of several weeks. This suggests that its origin was not a permanent deprivation phenomenon, but rather a matter of irritation or temporary deprivation resulting from débris from the lesions. Its course is strikingly comparable with that of epileptic seizures that occasionally follow extirpation of portions of the motor cortex, in that they also make their appearance a few days following the operation, gradually become more intense and eventually disappear. A localized seizure of the right side of the face occurred in monkey 6. The first seizure, seen on the third day after operation, consisted of a tic of the eyelid. Later the convulsions involved the whole facial musculature on that side and spread slightly to the opposite side. At

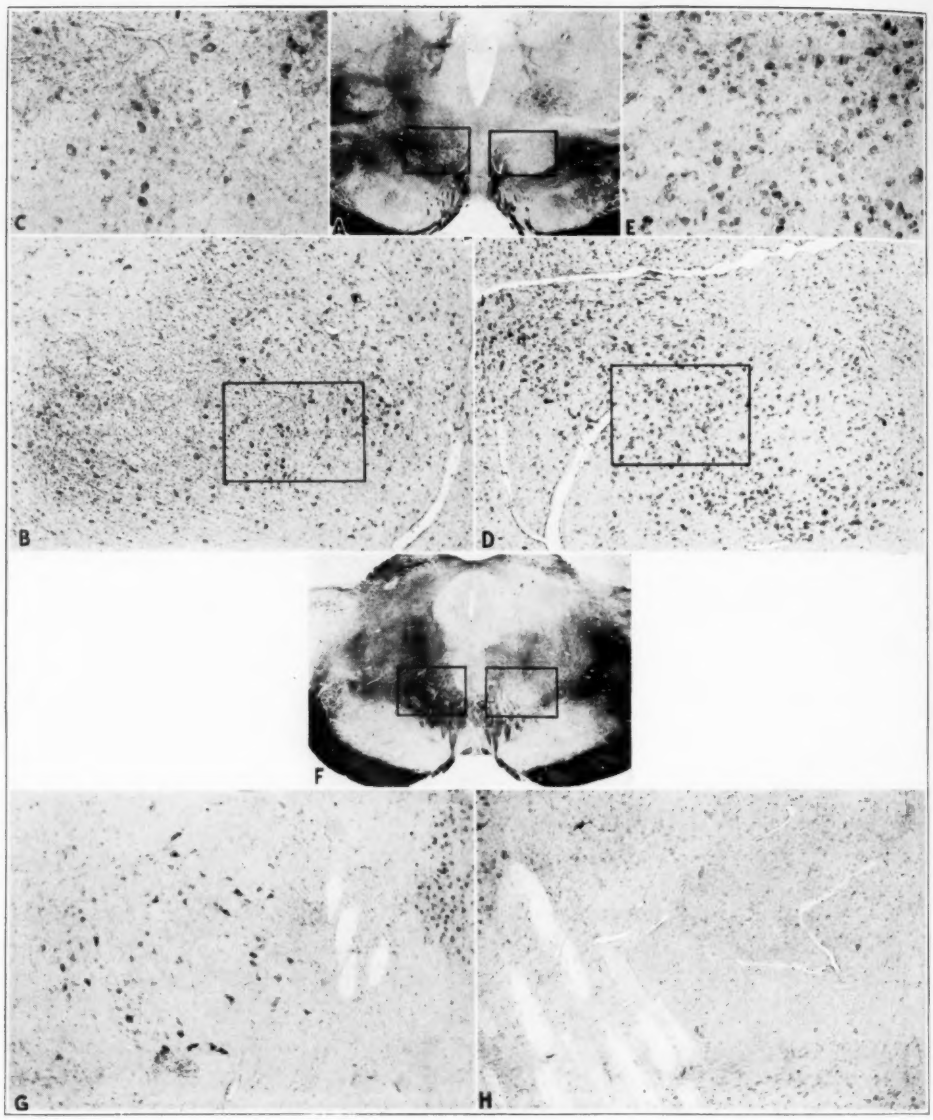

Fig. 5.—Photomicrographs of sections through the red nuclei in the brain of monkey 6: *A*, from a section at approximately the middle level of the small cell red nucleus. The gray matter of the nucleus on the left is readily seen with its capsule of fibers. On the right side the area of the gray matter is considerably enlarged, because of the degeneration of the fibers in the capsule which come from the brachium conjunctivum. *B*, from the area within the left square in *A*, the section having been stained with neutral red previous to the staining for fiber tracts. Note the sparsity of cells here as compared with those in *D*. *C*, from the area within the square in *B*. Compare with *E*. D, from the area within the right square in *A*, taken after staining with neutral red. Compare with *B*. *E*, from the area within the square in *D*. Compare with *C*. *F*, from approximately the middle level of the large cell red nucleus. Note that on the left this nucleus is indicated by only a slight amount of gray matter. The cells themselves are in the main embedded between the fibers of the brachium conjunctivum. On the right the absence of the brachium conjunctivum is evident. *G*, from the area within the left square in *F*. Note the presence of two types of cells; one large and stained very heavily, the other somewhat smaller and stained more lightly, the Nissl granules being apparent. The section was stained with neutral red previous to staining for fiber tracts. *H*, from the area within the right square in *F*. Note the complete absence of cells.

their height they were precipitated by the attempt to chew. There was no paralysis of the right side of the face, and histologic examination of the brain stem showed intact facial nuclei.

Righting Reactions and Muscle Tone: The bilateral elimination of the rubral systems in monkey 12 without interfering with any of the righting reflexes and with no disturbance in postural muscular tone demonstrates conclusively that these functions are not dependent on the integrity of the red nuclei.

The permanent slight asymmetry in righting which was present in monkeys 6 and 8 following lesions that involved a medial quarter segment in addition to the lateral segment indicates that in the monkey, as in the cat and dog, the cephalic central righting mechanisms course to some extent, if not predominantly, in the medial quarter segments. The experiment on monkey 5 certainly adds suggestive evidence for this conclusion. This experiment is, however, open to the criticism that although only the medial quarter segments were destroyed anatomically, one does not know in an acute experiment the extent of a functional section. It is for this reason that it is not permissible to draw conclusions on localization of function from experiments in extirpation in which dysfunction results unless a permanent deprivation syndrome occurs.

Anatomic Considerations.—The fact that the majority of the cells in the ipsilateral cephalic red nuclei degenerate following section of the lateral quarter segment in the pons demonstrates that the axis-cylinders from these cells course uncrossed, as far caudally as the pons, in a lateral position in the stem (figs. 1 and 2). It may be that the axis-cylinders of the undegenerated cells course cephalically, since they do not degenerate following a total hemisection (figs. 3 and 5) or after bilateral section of the lateral quarter segments in the pons. The only other possible course would be that they cross and pass down in the medial quarter segment, or that they terminate a short distance below the nucleus above the level of the lesion.

It was a surprise to us to find that the brachium conjunctivum did not degenerate proximal to the lesion, particularly since we had anticipated that degeneration would occur and thus demonstrate the exact source of origin of the fibers passing in this peduncle.

SUMMARY AND CONCLUSIONS

1. The bilateral rubral systems are not essential for normal coordination of muscular movements, static muscular stability, normal righting reactions and normal integration of postural muscle tone.

2. It is not essential that a brachium conjunctivum be intact for normal homolateral coordination of muscular movements and static muscular stability.

3. Transverse section of the lateral quarter segment of the brain stem at a level in the caudal part of the pons results in degeneration of all cells in the contralateral large cell red nucleus and of the majority of the cells in the ipsilateral small cell red nucleus.

4. Although eight months after section of a brachium conjunctivum there was complete degeneration of the fibers distal to the section, there was only a slight thinning of the bundle proximal to the lesion. Retrograde degeneration of cells in the cerebellar nuclei did not result except in the cephalic part of the nucleus emboliformis where they had completely disappeared.

Clinical Notes

PARAPLEGIA OF PREGNANCY (SUBACUTE COMBINED DEGENERATION OF THE CORD)

A Clinicopathologic Study

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Of the neuropsychiatric episodes of pregnancy, the best known are the psychoses. Aside from accidental cerebral complications (hemorrhage, thrombosis, embolism), disturbances of the central or peripheral nervous system proper, that is, pure organic nerve lesions, are relatively rare. For the most part the lesions are in the peripheral nerves and are classified either as pressure neuritis—that is, they result from pressure by the pregnant uterus on the sacral plexus—or as polyneuritis. Lesions of the spinal cord are uncommon. According to Hösslin,[1] who enumerated nearly every conceivable disease of the spinal cord as a possible direct or indirect complication of pregnancy, the most frequent form seems to be "transverse" or "compression" myelitis. However, neither Hösslin nor later observers (Berkwitz and Lufkin,[2] for instance) described subacute combined degeneration of the cord as a complication of pregnancy, regardless of the fact that pregnancy is frequently associated with anemia. So far as we could ascertain, so-called anemic changes in the cord in pregnancy have been alluded to only occasionally in the literature (Strauss,[3] Naegeli,[4] Felo[5]), and have not been described. Thus, according to Felo, the spinal cord is seldom affected in "anemias of pregnancy." If it is, the changes never attain the extent observable in the cryptogenic, ordinary idiopathic form of anemia. Naegeli found that the spinal cord may become involved in the early stages of the anemia of pregnancy, while Russel, Batten and

From the Neurologic Service, Research and Educational Hospital, and the Division of Neuropathology, University of Illinois College of Medicine.

1. Hösslin, R.: Die Schwangerschaftslähmungen der Mütter, Arch. f. Psychiat. **38**:730, 1904; **40**:445, 1905.

2. Berkwitz, N. J., and Lufkin, N. H.: Toxic Neuronitis of Pregnancy: A Clinico-Pathologic Report, Surg., Gynec. & Obst. **54**:743, 1932.

3. Strauss, M. B.: The Etiology and Treatment of Anemia in Pregnancy, J. A. M. A. **102**:281 (Jan. 27) 1934.

4. Naegeli: Ueber perniciöse Anaemie, Klin. Wchnschr. **9**:1843, 1930.

5. Felo: Ueber die Schwangerschaftsperniziosa, Folia haemat. **44**:446, 1931.

Collier [6] observed in two cases that the early symptoms of subacute combined degeneration of the cord appeared after pregnancy.

In the case to be recorded the changes in the spinal cord of a pregnant girl were outstanding and of sufficient significance to warrant a special study.

REPORT OF A CASE

History.—A white girl, aged 19, was admitted to the Research and Educational Hospital of the University of Illinois, on Jan. 19, 1933. She had been an inmate of a state training school for girls, and had had gonorrheal vaginitis, conjunctivitis, bilateral keratitis and syphilis at the age of 15. At that time the Kahn reaction of the blood was two plus, and she received twenty-four injections of neoarsphenamine, twenty-four injections of bismuth, and inunctions of mercury and potassium iodide by mouth weekly. Five days before admission the patient had a "sore throat and pharyngitis," pain in the lumbar part of the spine, tingling, numbness, weakness and shooting pains in the legs and an elevated temperature. The foregoing symptoms were followed within three days after the onset by complete paralysis of the lower extremities and urinary incontinence. According to the records at the training school, the paraplegia was associated with loss of sensibility for pain and temperature up to the level of the umbilicus, while the senses of vibration, position and touch were preserved. The tendon reflexes were exaggerated in the upper and diminished in the lower extremities; the cranial nerves, including the pupillary reaction, were normal. Examination of the blood and spinal fluid gave negative results.

Examination.—The patient was pale, poorly nourished and pregnant; the lower extremities were completely paralyzed. The paraplegia was flaccid; the muscles of the paralyzed extremities were flabby; active movements were abolished, and passive movements were not resisted. The tendon reflexes were lost, and a Babinski sign was suspected on the left. The upper abdominal reflexes were present, with a positive Beevor sign. There were: hypalgesia, especially on the left leg, extending upward to the level of the umbilicus; normal vibratory, position and tactile sensibilities; absence of glossitis and trophic disturbances, and the presence of corneal opacity on the left. A systolic murmur was heard over the heart, but was not transmitted to the left axilla. No anomalies were found in the upper extremities, cranial nerves, pupils, ocular fundi, speech or mental condition. There was no retention of urine; the specific gravity was 1.016; the urine was cloudy and contained many pus cells and albumin, one plus. Examinations of the blood and spinal fluid gave negative results; the Pandy test was faintly positive; there were 4 cells in the spinal fluid; the Lange test was negative. The temperature was 98.5 F.; the pulse rate, 80, and the respiration rate, 20.

Course.—The condition of the neurologic signs was somewhat changeable. The knee jerks, for instance, became lively and the Babinski, Chaddock and Rossolimo signs became positive, while the achilles tendon jerks became lost. Spontaneous jerkings in the lower extremities appeared, and marked defense reflexes were obtainable; forced flexion of the big toes caused a rapid and forceful flexion of the corresponding knee and hip joints. Three weeks after the onset of the paralysis, extensive bed sores developed around the sacrum, and a septic fever (105 F.) set in (February 7), accompanied by chills and a pulse rate of 140. The blood pressure varied from 102 systolic and 55 diastolic to 85 systolic and 50

6. Russel, J. S.; Batten, F. E., and Collier, J.: Subacute Combined Degeneration of the Spinal Cord, Brain **23**:39, 1900.

diastolic. Lumbar puncture always revealed absence of a spinal block, normal pressure and a normal number of cells (4 cells per cubic millimeter); the total protein and globulin (Pandy test, one plus) were also within normal limits. The Wassermann test was always negative. The colloidal gold curve was 00000000. Roentgen examination of the vertebral column revealed no anomalies. Repeated examinations of the blood showed: hemoglobin, from 75 to 50 per cent; red cells, from 4,300,000 to 2,200,000; white cells, from 15,550 to 4,600, with 74 per cent polymorphonuclears and 25 per cent lymphocytes. Staphylococcus albus was isolated from the blood. Examination of the urine gave practically negative results. No report of an examination of the stomach contents for acidity was found in the record.

Dr. F. H. Falls, of the obstetric department, found no indication for interrupting the pregnancy. A painless, premature delivery occurred on April 8, 1933. Nevertheless, the condition of the patient grew steadily worse because of the septic condition and extensive bed sores. Death occurred ten days after delivery.

Diagnosis.—The difficulties in diagnosis were great. The acute onset of the paraplegia after a febrile sore throat suggested a myelitis; the history of syphilis also suggested syphilis of the cord, while the anemia suggested the possibility of so-called anemic changes in the cord. On several occasions the clinical findings suggested a Brown-Séquard paralysis from pressure on the spinal cord, but the further course of the disease, which was complicated by pregnancy and sepsis, made the diagnosis obscure.

Antisyphilitic therapy was first administered, but was soon discontinued and replaced by a diet rich in protein, with iron and cod liver oil; blood transfusion was done in the later stages of the disease.

Necropsy (April 18, 1933).—Macroscopic Observations: There were: large decubitus ulcers of the sacrum and promontories of the hips, with multiple abscesses in the floor of the ulcers and extension through the sacral hiatus into the epidural spaces of the sacral canal; embolic abscesses in the lungs and posterior wall of the left ventricle and kidneys; septic infarcts in the spleen; old, healed mild endocarditis; concentric hypertrophy of the heart; recent vegetative endocarditis; a puerperal uterus; hydronephrosis of the right and a double ureter of the left kidney.

Microscopic Observations: The spinal cord exhibited marked degeneration of the lateral columns (fig. 1). The pyramidal and spinocerebellar tracts were especially involved; very few healthy fibers were seen in these tracts or in the areas adjoining the posterior horns. The anterior columns were better preserved, but the sulcomarginal tract of Löwenthal was much degenerated. In Weigert specimens the posterior columns showed pale areas, which in specimens stained by the Alzheimer-Mann method appeared darker (fig. 1).

The degenerated areas of the lateral columns were vacuolated (figs. 1 and 2); the majority of the vacuoles were empty, but in some there were various gliogenous elements, mainly myeloclasts and myelophages. The former were exceptionally numerous, and some vacuoles harbored two or more such elements; they were granular, always exhibited minute granules of lipoids when stained with scarlet red and contained a pyknotic nucleus, which was displaced to the periphery. The myelophages were larger and contained fairly large vacuoles, many of which harbored minute fragments of myelin or of axons. The myelophages also were numerous and occasionally were mixed with gitter cells of various types. The gitter cells always contained lipoids; some parts of the microscopic field in which

such cells were especially numerous, appeared red when stained with scarlet red or black when stained by the method of Marchi. Such fields, however, were very small (fig. 2); the larger fields exhibited the earliest stages of nerve degeneration. Cytoplasmic astrocytes, though present, were few. In longitudinal sections the changes appeared much more clearly. As is seen in figure 3, the vacuolated portion clearly exhibited strands of glial tissue which formed meshes enclosing various glial elements. Very few axons or myelin sheaths could be discerned; the greater number of them had been broken up and lodged within myeloclasts and myelophages, or had already been transformed into fatlike substances.

In contrast to such definitely degenerative changes in the lateral columns, which were especially well marked in the thoracic region and much less in the

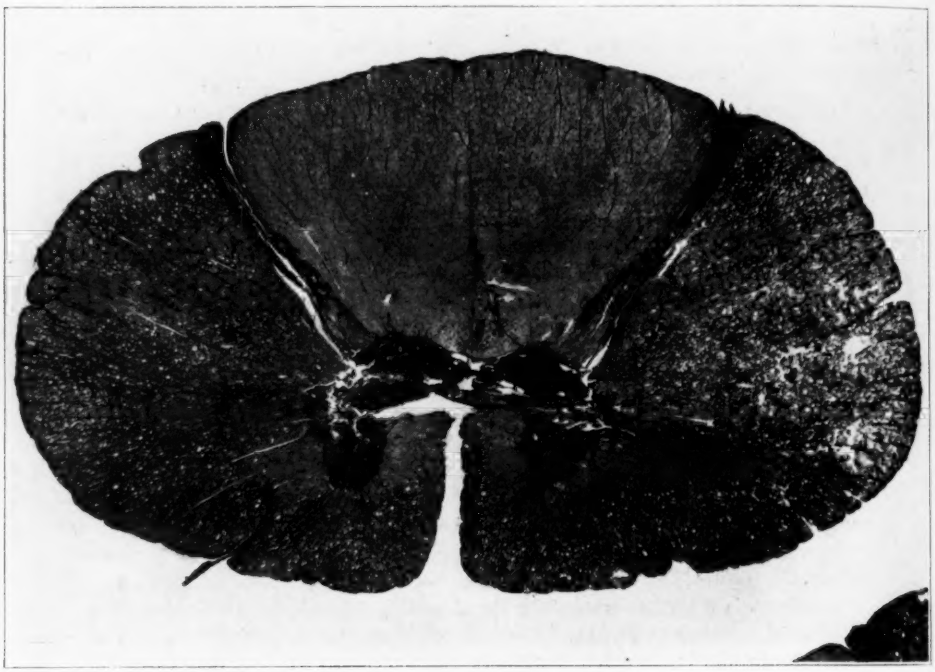

Fig. 1.—Third thoracic segment. The lateral columns, including the pyramidal and the spinocerebellar tracts, and the sulcomarginal tract of the anterior columns are degenerated. Some median fibers of the posterior columns appear more darkly stained than the lateral portions of the columns of Burdach. The degenerated areas are reproduced in longitudinal section in figures 3 and 4 (Alzheimer-Mann stain).

cervical and lumbosacral regions, the posterior columns exhibited only mild changes. These could be detected only after careful study of specially stained specimens, though the posterior columns appeared changed even macroscopically. Thus, in Weigert-Pal specimens they exhibited in the center a pale area, which in specimens stained by the Alzheimer-Mann method appeared rather dark. In longitudinal sections, the dark areas stained by the Alzheimer-Mann or Jakob-Mallory method revealed fragments of myelin still in situ, anchored, as it were,

in the tissues, thus preserving the architecture of the columns (fig. 4). The nerve fibers, in general, appeared swollen or vacuolated when stained by the method of Bielschowsky (fig. 4 *B*). Regardless of the staining method used, the posterior columns appeared by no means normal. Like the lateral columns they were degenerated; there existed, therefore, a condition that may be designated as a

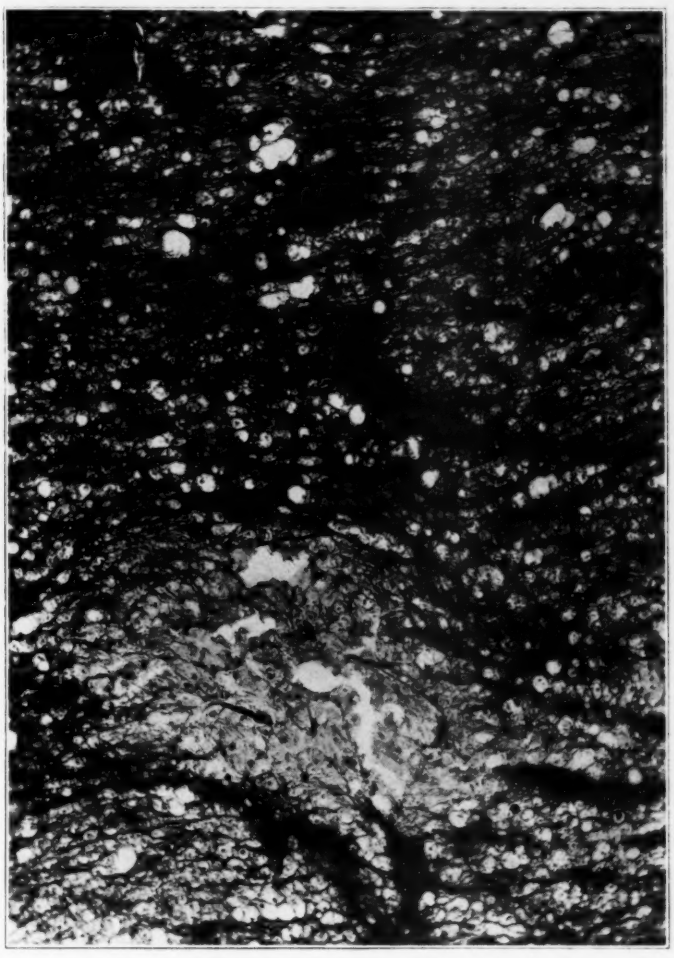

Fig. 2.—A focus of degenerative softening (large, light area in the lower part of the picture), consisting of gitter cells. The dark strands are glia fibers. Some vacuoles contain degenerative products (Alzheimer-Mann stain).

combined degeneration of the lateral and posterior columns. The majority of the fibers of the posterior columns were not affected, this probably being the reason for the preservation of the senses of vibration, touch and position, and the predominance of hypalgesia and signs of involvement of the pyramidal tracts. The anterior columns exhibited changes similar to those in the lateral columns.

The gray matter was practically normal in the thoracic and cervical regions. In the lumbosacral segments the ganglion cells of the anterior horns were swollen (fig. 5) and devoid of dendrons; their nuclei were displaced to the periphery; the Nissl bodies were in dustlike fragments and gathered at the periphery of the cell. In short, the ganglion cells presented a condition that is generally described as axonal reaction; this has been well pictured by Berkwitz and Lufkin [2] in cases of polyneuritis of pregnancy. The spinal roots revealed no abnormalities. Changes also

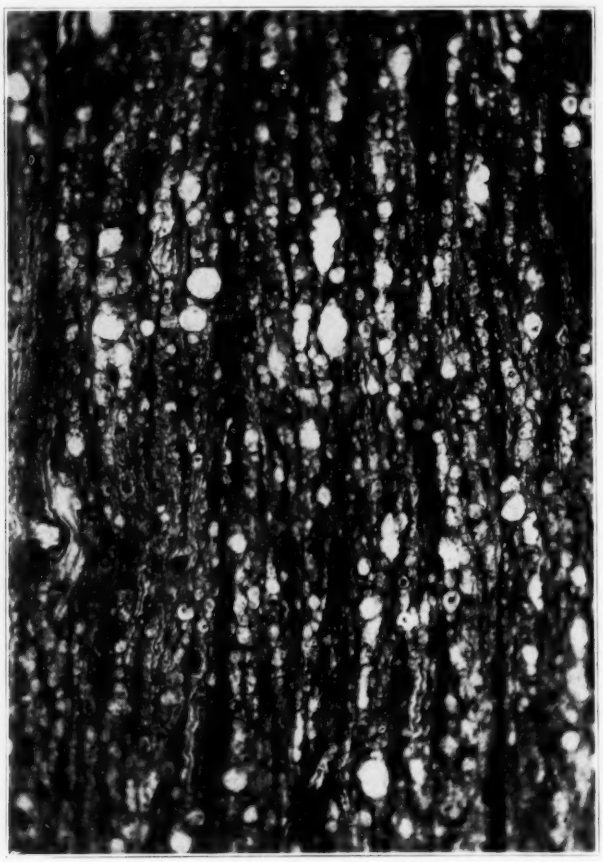

Fig. 3.—Longitudinal section of a degenerated lateral column. Some of the vacuoles are empty; the majority contain products of nerve degeneration which are described in the text (Alzheimer-Mann stain).

were absent or were mild in the cortex cerebri, basal ganglia, pons and medulla. In these regions, as in the gray and occasionally in the white substance of the spinal cord, marked inflammatory infiltrative phenomena were present, with many microglia cells and proliferated capillaries. The blood vessels, especially the small ones, were infiltrated with lymphocytes and polymorphonuclear cells (fig. 5); in addition, there were numerous scattered nodules consisting of glia cells mixed with

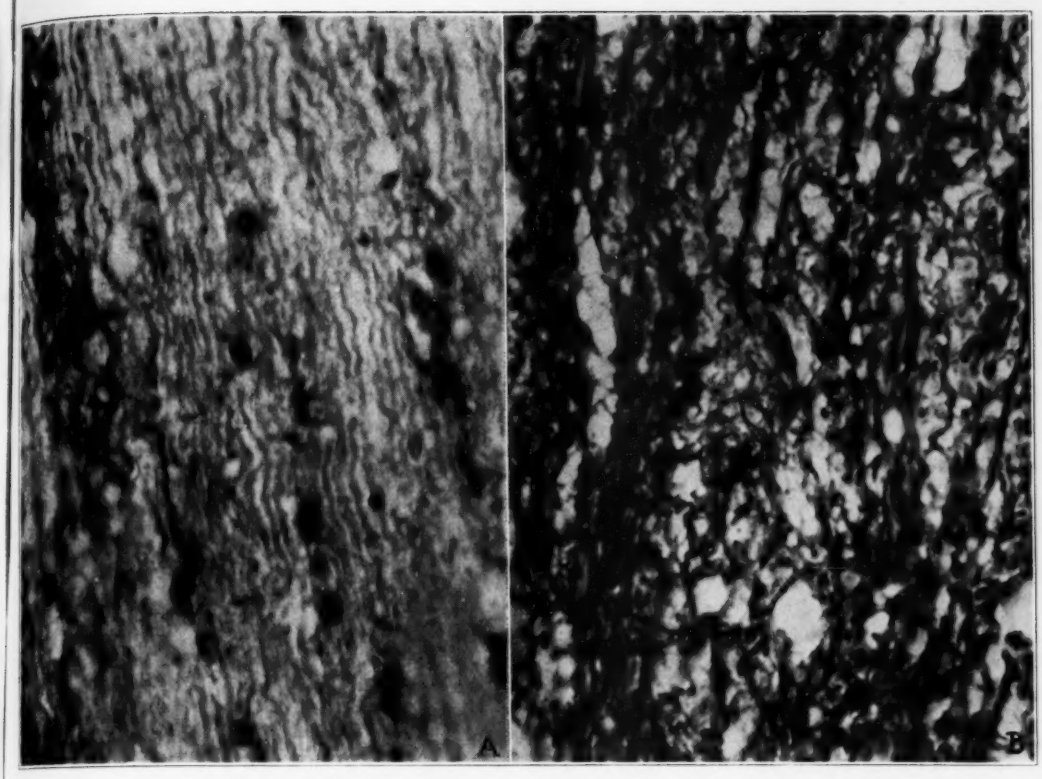

Fig. 4.—Longitudinal section of the darker areas in the posterior columns. *A*, fibers stained by the Alzheimer-Mann method. The axons are retained; their pale myelin sheaths are swollen, and the numerous dark bodies are cytoplasmic astrocytes containing distinct nuclei which are rich in chromatin. *B*, similar area stained by the method of Bielschowsky. The axons here are also well shown; the myelin is represented by the numerous pale, swollen formations.

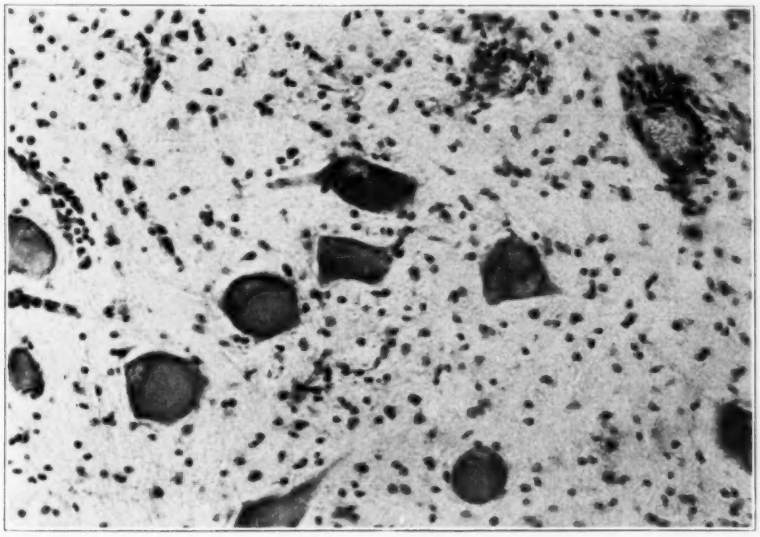

Fig. 5.—Anterior horn cells of the lumbosacral region of the cord. They exhibit so-called "axonal reaction"; infiltrated blood vessels are seen at the right and in the upper part (toluidine blue stain).

polymorphonuclears. The nodules exhibited the changes that have been described by Diamond [7] in cases of septicopyemia and were undoubtedly due to the severe septic state.

The meninges presented striking reactive phenomena; over the temporal lobe they contained many mesothelial cells, polyblasts, histiocytes, fibroblasts and some lymphocytes mixed with polymorphonuclear cells, which predominated in some areas.

SUMMARY AND COMMENT

In a young woman with a history of gonorrheal and syphilitic infections there developed suddenly, in the second trimester of pregnancy, a paraplegia with urinary, sensory and trophic disturbances associated with secondary (hypochromic) anemia and complicated by a fatal septicopyemia; degenerative changes were found in the spinal cord, with widespread inflammatory phenomena throughout the brain and cord such as are seen in septicopyemia.

The changes in the cord were especially marked in the lateral columns, involvement of which may explain the clinical signs referable to the pyramidal tracts, especially in the early stages of the disease, and probably also the hypalgesia. The mild involvement of the posterior columns, which showed signs of beginning degeneration only, may explain the presence of changes in the senses of vibration, touch and position. Had not attention been centered on the condition of the posterior columns, their involvement could easily have been overlooked, just as in some cases of combined involvement of the tracts of the spinal cord degeneration of the lateral columns may be so mild as to be overlooked. The changes were not those of syphilis or of inflammation, or those that occur in epidural lesions. They were degenerative, of the type observed in subacute combined degeneration of the spinal cord; they resembled nothing else. Probably the name "subacute funicular myelopathy," used by Globus and Strauss [8] for subacute combined degeneration of the cord, would be more appropriate. However, this term by no means gives a better definition. It is certainly much less scientific, for a myelopathy may also mean multiple sclerosis, syringomyelia, poliomyelitis and other lesions of the spinal cord. The immense numbers of myeloclasts and myelophages in the affected columns indicate a very early stage of the disease—several weeks' duration—as would be judged from the results of experimental observations. The changes thus correspond with the history of the onset, course and clinical picture in general.

In this case there was not the usual combination of subacute combined degeneration of the cord with pernicious anemia, achylia gastrica and glossitis. Certain laboratory examinations, for instance, determination of the gastric activity, could not be carried out because of the patient's condition, but the presence of hypochromic (secondary) anemia was certainly suggestive. One may presume that the anemia was of pernicious type, but it was either in the early stages or not sufficiently advanced to produce the specific changes in the blood seen in pernicious anemia. Naegeli [9] has stated that the changes in the blood typical of pernicious anemia occur only in some cases of the anemias of pregnancy. In other cases the changes are atypical, or the macrocytosis is so slight that even

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7. Diamond, I. B.: Changes in the Brain in Pyemia and Septicemia, Arch. Neurol. & Psychiat. **20**:524 (Sept.) 1928.

8. Globus, J. H., and Strauss, I.: Progressive Funicular Myelopathy (Subacute Combined Degeneration), Arch. Neurol. & Psychiat. **8**:366 (Oct.) 1922.

9. Naegeli: Ueber Frühstadien der perniziösen Anämie und über die Pathogenese der Krankheit, Deutsches Arch. f. klin. Med. **124**:221, 1918.

an experienced observer may have only a "suspicion" of the actual condition. He also said that because of the much shorter duration of the action of the toxin and the short duration of the anemia, even achylia gastrica and glossitis may be absent. Hence, though some anemias may be of the pernicious (macrocytic) type, typical changes in the blood may not be present. Anemia of pregnancy may thus differ little from the pernicious type, which probably would have developed in our case if time had permitted. Yet, it is due to the same toxins that are responsible for the changes in the spinal cord, and it is established that the latter may occur long before a typical pernicious anemia becomes apparent. The youth of our patient, the numerous infections—syphilitic, gonorrheal and staphylococcic—malnutrition and poor physical development may have accounted for the metabolic disturbances that were probably responsible for the changes in the spinal cord. At any rate, the changes were not those of myelitis or syphilis or such as are produced by epidural lesions. The clinical picture itself was overshadowed by the severe septic state, which caused additional changes such as occur generally in septicopyemia and were not related to the pregnancy.

CONCLUSIONS

1. Degenerative changes of the cord may occur during pregnancy.

2. They occur in the form of subacute combined degeneration of the cord and may affect the lateral more than the posterior columns and thus give a clinical picture of paraplegia.

3. Subacute combined degeneration of the cord, like anemias, may be a manifestation of toxemia of pregnancy and be caused by the same toxins that produce anemia and may run a very acute course.

4. Though the interruption of pregnancy in the presence of such marked irreparable changes in the cord may be of questionable value, its continuation is hardly permissible, for it cannot be expected to run a normal course.

FRIEDREICH'S DISEASE

A Report of Two Unusual Cases

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The two cases described in this paper are considered atypical forms of Friedreich's disease. The unusual feature in each case is the presence of exaggerated patellar and achilles reflexes, associated with clonus and a positive Rossolimo sign. This report offers some corroboration of the contention that a spastic form of Friedreich's disease exists. In considering the differential diagnosis, the validity of a diagnosis of Friedreich's disease in the presence of exaggerated patellar and achilles reflexes will be indicated.

REPORT OF CASES

CASE 1.—*History.*—Joseph H., aged 17, came to the outpatient neurologic service of the Illinois Research and Educational Hospitals in October 1933, complaining of difficulty in walking and unsteadiness of the hands. There was no history of disease of the nervous system in the mother's family. A cousin—a son of a paternal aunt—aged 29, was stoop-shouldered and stumbled and staggered in walking; sometimes he "shook all over" and fell to the ground "when excited." The father's whereabouts and present status were unknown. The mother and four siblings (two boys older and a girl and a boy younger than the patient) had good health. Twin brothers, aged 22, the eldest of the siblings, had a typical form of Friedreich's disease. They were admitted to Cook County Hospital in May 1920, where a diagnosis of Friedreich's disease was made. Later they were patients in the neurologic service of the Illinois Research and Educational Hospitals, where the diagnosis was confirmed. At present they are in the Oak Forest Infirmary, and according to a recent report exhibit all the characteristic signs of Friedreich's disease. The cases were reported by Hess.[1]

The patient was born at term and was breast fed. When he was 2 years of age he and all the other children in the family had influenza (1918). All recovered quickly except the twins, who soon began to show ataxia, and gradually other signs of Friedreich's disease. The patient, however, remained well until the age of 10, when it was observed that his hands were unsteady while carrying liquids to the table. Three years later he began to stumble and fall frequently when walking. The difficulty in walking gradually increased, and during the past year the unsteadiness of the hands had become more severe.

Examination.—The patient was large for his age and well nourished. The left shoulder and hip were elevated; there was a "pigeon breast" deformity of the chest, and scoliosis with the convexity to the left in the thoracic and to the right in the lumbar region. On standing the shoulders were stooped and the patient swayed back and forth. The face was mobile; vision was normal, and the teeth

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From the Department of Neuropsychiatry, University of Illinois College of Medicine.

1. Hess, J. H.: Friedreich's Ataxia in Twin Boys, M. Clin. North America **5**:1749, 1921-1922.

were in good repair. There were no abnormalities of the heart or lungs. The feet were cold but not cyanotic and exhibited no deformities. The pupils were round, equal and regular, and reacted well to light and in accommodation. Fine horizontal nystagmoid movements were occasionally present when the eyes were turned well outward. There were no ptosis and no disturbance of ocular movements. The patient could close each eye separately without difficulty. The corneal and conjunctival reflexes were present; the jaw jerk was absent. The tongue was protruded in the midline, could be moved to the right or left and showed no tremor. Palatal and pharyngeal reflexes were present. Muscular development was good, and muscular strength was conserved in all extremities. There were no atrophies or paralyses. Active movements of the hands were markedly ataxic. This was demonstrated in finger-to-finger and finger-to-nose tests, in writing, etc. The handwriting was irregular and tremulous. There were, however, no intention tremor and no dysmetria. Rapid alternating movements of the hands and arms were performed slowly and clumsily (adiadokokinesis). On attempts to arise from the supine position, the movements of the trunk were clumsy but not ataxic. The lower extremities were slightly spastic. The heel-to-knee test was performed slowly but accurately. In walking, the shoulders were stooped and the gait was staggering, very ataxic and slightly spastic, with stumbling to either side. The Romberg sign was positive. The patellar and achilles reflexes were exaggerated; the biceps reflex was absent; the triceps, radial and cremasteric reflexes were present; the abdominal reflexes were absent in the upper and present in the lower quadrants. Ankle clonus, not sustained, was elicited on the left side. There was a Chaddock sign on the left, and Babinski and Rossolimo signs were present bilaterally. Articulation was slow and scanning. Sensation was intact except for a slight disturbance of kinesthesia in the toes, which were insensitive to small changes in position. The fundi were normal. Intelligence was average.

CASE 2.—*History.*—Dan H., aged 17, was seen Nov. 16, 1933, when he complained of difficulty in walking for one year, a difficulty which had gradually increased. There was no history of disease of the nervous system in the family. The father, mother and siblings were living and well. When young the patient had had diphtheria, measles and chickenpox. Otherwise he had had good health until the onset of the disturbance of gait.

Examination.—The patient was well developed and nourished. General examination gave essentially negative results except for bilateral pes cavus and a left hammer toe. There was no scoliosis. The pupils were equal and regular, and reacted to light and in accommodation. There was a fine, rapid, vertical nystagmus on upward gaze and a bilateral horizontal nystagmus on turning the eyes laterally. No disturbance of the ocular movements was present. The corneal and conjunctival reflexes were easily elicited, and the jaw jerk was present. There was a fine tremor of the protruded tongue, but there was no deviation from the midline. The palatal and pharyngeal reflexes were present. Muscular strength was good in all extremities, and there were no atrophies or paralyses. Active movements of the arms were ataxic in finger-to-finger and finger-to-nose tests, but there was no asynergy, dysmetria or adiadokokinesis. The lower extremities were markedly spastic. In performing the heel-to-knee test the movements were bilaterally ataxic. The patient walked on a wide base with a swaying, spastic-ataxic gait, the ataxic component being especially prominent. The Romberg sign was positive. All the tendon reflexes were exaggerated, especially the patellar and achilles jerks. The abdominal and cremasteric reflexes were absent. Patellar

clonus was elicited bilaterally, but was inconstant on the left side. Sustained ankle clonus was elicited on the left side; on the right it was exhaustible. Chaddock, Babinski, Rossolimo and Mendel-Bechterew signs were present bilaterally. Speech was scanning and explosive. Sensation was intact. The fundi were normal. Intelligence was average.

COMMENT

The unusual features in these two cases were the exaggerated patellar and achilles reflexes, clonus and Babinski and Rossolimo signs. The literature, however, contains several reports of patients with Friedreich's disease whose patellar reflexes were preserved or exaggerated. Mingazzini [2] described the case of a patient whose patellar reflexes were "lively." Menzel's [3] patient, in addition to exaggerated patellar reflexes, had many other symptoms similar to those in my patients, such as unsteady, reeling and slightly spastic gait, ataxia of the hands and slow, poorly articulated speech. At autopsy, the pathologic changes in the spinal cord of this patient were those of Friedreich's disease. Clarke,[4] Frey,[5] Hodge [6] and Marqulies [7] also described patients with exaggerated patellar reflexes. Clarke described the knee jerks of his patient as "lively—perhaps brisker than normal." There was, however, no exaggeration of the deep reflexes of the arms. Cases in which the patellar reflex was conserved but not exaggerated were described by Clarke,[4] Combes [8] and Frey.[5]

In considering the differential diagnosis, Marie's heredocerebellar ataxia, Pelizaeus-Merzbacher [9] disease and multiple sclerosis must be mentioned. Oppenheim [10] has indicated that Marie's heredocerebellar ataxia, in which the tendon reflexes may be normal or exaggerated, frequently cannot be absolutely differentiated from Friedreich's disease on the basis of either the symptomatology or the pathologic variations. In the former disease, however, there may be ocular disturbances, such as oculomotor paralyses, optic atrophy and occasionally immobile pupils. Although oculomotor paralyses may occur in Friedreich's disease, they do so rarely. Intention tremor also occurs in Marie's heredocerebellar

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2. Mingazzini, G.: Weitere Beiträge zum Studium der Friedreichschen Krankheit, Arch. f. Psychiat. **42**:917, 1907.

3. Menzel, P.: Beitrag zur Kenntnis der hereditären Ataxie und Kleinhirnatrophie, Arch. f. Psychiat. **22**:160, 1891.

4. Clarke, J. M.: A Case of Friedreich's Disease or Hereditary Ataxia with Necropsy, Brit. M. J. **2**:1294, 1894.

5. Frey, K.: Zwei Stammbäume von hereditärer Ataxie, Deutsche Ztschr. f. Nervenh. **44**:351, 1912.

6. Hodge, G.: Three Cases of Friedreich's Disease All Presenting Marked Increase of the Knee-Jerk, Brit. M. J. **1**:1405, 1897.

7. Marqulies, A.: Ein Beitrag zu den Uebergangsformen zwischen Friedreich'scher Ataxie, und der Heredo-Ataxie cérébelleuse von Marie, Inaug. Dissert., Berlin, S. Scholem, 1901; cited by Mingazzini, G., and Perusini, G.: J. Ment. Path. **6**:105, 1904.

8. Combes, P.: Maladie de Friedreich. Essai historique, anatomo-clinique et physiologique, Thèse de Montpellier, 1902, p. 78; cited by Mingazzini, G. and Perusini, G.: J. Ment. Path. **6**:105, 1904.

9. Merzbacher, L.: Eine eigenartige familiär-hereditäre Erkrankungsform, Ztschr. f. d. ges. Neurol. u. Psychiat. **3**:1, 1910.

10. Oppenheim, H.: Text-Book of Nervous Diseases, ed. 5, London, Foulis, 1910, p. 198.

ataxia; neither of my patients exhibited a tremor of this type. In view of the close similarity of these two diseases, however, the possibility that the condition of my patients is a transitional form between them must be considered.

Pelizaeus-Merzbacher disease ("hereditary familial multiple sclerosis" of Pelizaeus [11]) has many symptoms in common with those of my cases, such as exaggerated tendon reflexes, ataxia of the extremities, slow, scanning speech, intact sensibility, clonus, positive Babinski, Rossolimo and Mendel-Bechterew signs, spasticity of the legs and staggering gait. This disease, however, can easily be excluded, mainly by the history, because the symptoms appear during the first year of life. The first sign usually is nystagmus; intention tremor occurs; there is remission of some symptoms, and spasticity of the legs is severe, soon interfering with walking and resulting in extreme contractures. Temporal pallor of the optic disks also occurs, but this sign is considered as nonspecific by Bostroem.[12] The abdominal reflexes may be absent in both this and Friedreich's disease.

Both my patients had many symptoms in common with those of multiple sclerosis, such as nystagmus, slow, scanning speech, spastic-ataxic gait, exaggerated tendon reflexes and absent abdominal reflexes. Neither patient, however, exhibited any change in the optic disks, oculomotor paralyses, intention tremor or emotional changes. It is particularly difficult to exclude multiple sclerosis in case 2, because of the striking exaggeration of all of the tendon reflexes, ankle and patellar clonus, positive Babinski, Chaddock, Rossolimo and Mendel-Bechterew signs and absence of abdominal reflexes. Nevertheless, the first manifestation exhibited by this patient was the fundamental sign—marked ataxia of the legs, without paralysis—whereas in multiple sclerosis the initial symptom usually is spasticity of the lower extremities. Also, the patient had bilateral pes cavus and a hammer toe which, although not absolutely pathognomonic of Friedreich's disease, are typical of it and do not occur in multiple sclerosis. In addition, speech, though scanning, had also the explosive character of that in Friedreich's disease; the age at which the disease began, 16, was young for multiple sclerosis. The latter condition is, however, the most difficult to differentiate, especially in the absence of a good and reliable history.

The two cases show that the pyramidal tract may be involved in Friedreich's disease more intensely than any other system of spinal cord fibers, in contrast to an opinion held by some older observers [13] who were skeptical about the anatomic lesion of the pyramidal fibers in this morbid condition.

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11. Pelizaeus, F.: Ueber eine eigenthümliche Form spastischer Lähmung, mit Cerebralerscheinungen auf hereditärer Grundlage (Multiple Sklerose), Arch. f. Psychiat. **16**:698, 1885.

12. Bostroem, A.: Ueber die Pelizaeus-Merzbachersche Krankheit, Deutsche Ztschr. f. Nervenh. **100**:63, 1927.

13. Marie, P.: Vorlesungen über die Krankheiten des Rückenmarkes, translated by Max Weiss, Leipzig, Franz Deuticke, 1894, p. 425.

PAROXYSMAL HYPERTONIA INDUCED BY AFFECT

A Symptom in Man and in Lower Animals

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Throughout this paper I shall use "affective hypertonia" as a designation for paroxysmal hypertonia occurring in response to sudden strong affect. While affective *hypotonia*, or cataplexy, is well known, a survey of the literature shows that affective *hypertonia* has received scant attention. I shall describe the phenomenon as it occurs in man and in certain lower animals and shall state the conclusions that seem, at the present time, deducible regarding its pathogenesis. In affective hypertonia, as in cataplexy, consciousness is unimpaired.

THE PHENOMENON IN LOWER ANIMALS

OBSERVATIONS ON GOATS

The most striking occurrence of affective hypertonia is in a breed of goats found in certain parts of Alabama, Tennessee, Kentucky and Texas. My attention was drawn to them by a reference in an article on Alabama by Simpich.[1] Mr. R. J. Goode, of Alabama, the owner of the goats referred to in the aforementioned article, generously supplied me with a detailed account of their behavior in response to affective stimuli. Subsequently I came across articles on the subject by White and Plaskett,[2] Dexler,[3] Hooper[4] and Lush.[5] From these sources is derived the following account of these remarkable goats.

In severe cases the afflicted goat, when startled or frightened, responds with generalized hypertonia of such degree that all its muscles on palpation feel "as hard as wood" (White and Plaskett). Passive flexion of the extremities is then impossible. The goat is utterly unable to move. The rigidity involves also the respiratory muscles, so that difficulty in breathing or even temporary cessation of respiration may occur. The posture is that of ordinary quadrupedal standing. "The head is held high and drawn upward. The same for the tail, although a goat's tail is always up anyway" (Goode[6]). Whether the animal falls depends on its relation to gravity at the moment of the onset of the attack: If the attack occurs when it is well balanced on all fours, it will remain standing; if, on the other hand, the attack catches it off balance, it will fall. Frequently the stiffness supervenes a fraction of a second after the goat has begun to move away from the source of the stimulus; in these instances, of course, it is apt to be caught off balance and may fall. If the goat is standing during an attack and one pushes it over on its side, *the quadrupedal standing posture is unchanged;* in other words, the goat then resembles a graven image placed on its side. In the

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1. Simpich, Frederick: Nat. Geog. Mag., Dec., 1931, p. 730.

2. White, G. R., and Plaskett, J.: "Nervous," "Stiff-Legged," or "Fainting" Goats, Am. Vet. Rev. **28**:556, 1904.

3. Dexler, H.: Die Schreckziegen oder Fainting Goats, Berl. tierärztl. Wchnschr., Dec. 31, 1908, p. 970.

4. Hooper, J. J.: A Peculiar Breed of Goats, Science **43**:571, 1916.

5. Lush, J. L.: "Nervous" Goats, J. Heredity **21**:243, 1930.

6. Goode: Personal communications to the author.

words of White and Plaskett, the animals are "so rigid and stiff that they can be lifted bodily without bending." The rigidity lasts from ten to twenty seconds, after which the animal begins to walk off. During the first 8 or 10 yards (7 to 9 meters), the legs, especially the hind legs, are still somewhat stiff and are moderately abducted, causing awkwardness of gait. Beyond that distance there is no longer any stiffness, and the animal is then entirely normal in its movements.

Loss of consciousness does not occur. Mr. Goode, who has observed these goats for over twelve years, wrote me that when he approaches a goat during an attack the animal shows unmistakable signs of following him with its eyes. "A threatening motion (made during the attack)...causes the goat to make an attempt to move away, but no more than a spasmodic effort results, because of the fact that the muscles are temporarily so stiffened that actual locomotion cannot be accomplished." White and Plaskett stated that during the attack the facial expression is one of "fright, anxiety, agony."

White and Plaskett reported that "it is said" that in rare instances goats have died during a severe attack. However, Lush was unable to find an actual instance of this sort. Dexler, who secured all his information from Dr. J. F. Gudernatsch of Cornell University, reported that death never occurred.

Clonic muscular movements do not occur, nor is there relaxation of the sphincters.

So far I have described only the severest attacks. In addition to these, there are milder forms in which the goat becomes rigid and motionless, but only for a "bare instant." It then moves off with stiff hind legs, gradually recovering, so that after 10 or 15 steps it runs normally. There are even milder instances in which there is not even momentary immobility, but only "momentary stiffness and dragging of the hind legs" (Lush).

Characteristically the attack occurs when the goat is startled, as by a loud, unexpected noise in its immediate vicinity or by the sudden appearance of an intruder. If the intruder approaches calmly and in full view of the goat, an attack seldom occurs. On the other hand, an attack *will* occur if the intruder approaches unobserved and then suddenly rushes up to the goat yelling and waving his arms. The response varies with the intensity of the stimulus. Thus, if a flock of the goats are moderately startled, some will react with attacks while others will be unaffected. On the other hand, if one startles them more severely one may, to quote Mr. Goode, "catch any goat in the flock before he is able to move. In such cases, some of them will stand rigidly without moving and others will fall down..... If one should arrange to get very close to them and then make a sudden appearance with noise or waving of arms, it is not unusual that *every* animal of the flock will fall down."

According to Lush, after a goat has been frightened into having an attack, he "usually cannot be frightened again, no matter how great the excitement may be, until he has had at least 20 to 30 minutes to rest." Mr. Goode has found the duration of this period to be fifteen or twenty minutes.

The only other effective stimulus consists of the effort to jump a moderately high fence or a moderately wide ditch. These goats cannot jump as well as normal goats (a fact of some economic importance—it is said that some farmers prefer them because the fence enclosing them need not be very high). The effort to execute what is to them a difficult jump will produce an attack. According to Goode, the effort to jump a 2-foot (0.6 meter) fence will produce this result; White and Plaskett reported that a 15 to 18 inch (38 to 45 cm.) fence will suffice. Lush reported that young kids will have an attack on attempting to jump

over even a stick or some other small object in the path. As regards horizontal jumping, the effort to jump a 2 foot ditch may produce an attack (Goode). This occurrence of hypertonia in response to voluntary muscular effort reminds one of the characteristic symptom of human myotonia. (Later, I shall refer to the occurrence of affective hypertonia in association with human myotonia.)

In view of the cases (to which I shall allude later) reported by Hughlings Jackson and others of patients who had attacks when unexpectedly touched, I asked Mr. Goode whether this ever occurred in the goats. He wrote in reply: "I have never had occasion to observe whether an attack could be produced by a touch when the goat is not expecting it, as my goats are not sufficiently tame to permit me to be near them without excitement."

Mr. Goode has often observed the goats fighting each other vigorously, but has never under these conditions seen an attack.

I questioned Mr. Goode on the following points: 1. Do agreeable emotions ever precipitate an attack? 2. Are there ever attacks of hypotonia instead of hypertonia? 3. Are any of the goats afflicted with morbid somnolence? To each of these questions he replied in the negative.

The malady is hereditary. In the early eighties a wanderer brought four afflicted goats into Marshall County, Tenn. Mr. Goode has made it a practice to try to trace the origin of every flock of afflicted goats coming under his notice and "without exception" has traced them back to this original quartet. His own goats were descended from a pair of afflicted goats purchased in Auburn, Ala. Every descendant of this pair has had the malady. He has not mated afflicted with healthy animals.

As to the age of onset, Mr. Goode stated that very young kids "often fail to show any indication of being affected, but as they grow older the characteristic becomes more and more marked, so that before the animal is one year old the characteristic is fully developed." White and Plaskett reported that a kid under their observation showed signs of the malady before it was 3 hours old.

Physically the goats are indistinguishable from normal goats. While sexual maturity is not late, they bear young only once a year. (The common goat usually has two sets of kids a year; some strains, however, such as the Angora, have one set a year.)

Excellent photographs, made during attacks, may be found in Lush's article and in Simpich's article on Alabama.

OBSERVATIONS ON SHEEP, HORSES AND CATTLE

Jones and Arnold[7] described a remarkable disease ("staggers") of sheep in Patagonia, characterized by paroxysmal hypertonia occurring when the animal is frightened. Their description of the seizure follows:

"At first sight the animal may appear normal. Excitement becomes great when the individual is alarmed by the barking of a dog, voices, etc. On becoming frightened it stands with a wild, excited look. The neck is extended and there is usually a marked trembling of the head. Muscular twitchings of the hind legs are a constant symptom; if the animal is driven it usually breaks into a panic-stricken run. After running a short distance, stiffness of the legs becomes marked. This stiffness is usually more noticeable in the hind legs. It moves with short, convulsive strides, and suddenly plunges forward, falling with the hind legs extended backward, and often rolls on its side. If the sheep falls on a

7. Jones, F. S., and Arnold, J. F.: Staggers in Sheep in Patagonia, J. Exper. Med. **26**:805, 1917.

hillside it is not unusual for it to roll over and over until a level plain is reached. It is quite common to observe a sudden stiffness of all four legs; when this occurs the individual may fall directly on its side. When the animal falls it displays extreme excitability; the eyes bulge and the pupils are dilated. The head is drawn back, the muscles of the neck are tense, and the legs are extended rigidly from the body, with the digits spread far apart. If a sharp sound is made the muscles become more rigid. If the sheep is permitted to lie undisturbed the muscles gradually become flaccid, and the animal rises to its feet with some difficulty and moves away, stiffly at first, but the gait soon becomes normal. If it is frightened the same phenomena are repeated."

From this it appears that the animal is conscious during the seizure.

A brilliant investigation by Jones and Arnold has revealed the cause of the malady. It occurs only in sheep which eat a certain toxic pampas-grass (Poa argentina), having been reduced to this necessity by shortage in the supply of nontoxic grass consequent on a period of drouth. Jones and Arnold were able at will to reproduce the disease by feeding sheep the toxic grass. Removal of this grass from the diet invariably led to complete cure. Liability to the disease is greatest during the first year of life.

The disease occurs also in horses and cattle under the same conditions as in sheep.

OBSERVATIONS ON GUINEA-PIGS

Cole and Ibsen[8] have found in newly born guinea-pigs a rapidly fatal disorder characterized by slow, irregular movements while the animal is at rest, clumsiness of gait and, later, inability to stand. Death results at the age of 1 to 2 weeks.

Affected animals show a striking reaction to sharp auditory stimuli. When an animal capable of standing is placed on its feet and a noise is made, it immediately "jumps upward and forward" on account of "sudden stiffening, particularly of the hind legs, then falls on its side, the whole body shaking to some extent, but the legs exhibiting strong clonic spasms. To the same stimulus normal individuals give merely a slight start, and then sit unconcernedly as before." The attack lasts a few moments.

In the severe stage of the condition attacks occur also following "attempts at voluntary movements of the hind legs."

Since it is not known whether consciousness is retained during the attacks, they can only tentatively be regarded as instances of affective hypertonia, in the sense in which that term is here used.

OBSERVATIONS ON PARROTS

Wilks[9] observed that "a sudden strange noise will cause my parrot to drop from its perch as if it had been shot." It is not known whether the animal was conscious and whether tone was increased.

THE PHENOMENON IN MAN

CASES IN THE LITERATURE

Some of the cases cited in this section are clearcut, by which I mean that it is fairly obvious that during the attack (1) the patient was fully conscious and (2) there was hypertonia. In the remaining cases there is some doubt on either or both of these points.

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8. Cole, L. J., and Ibsen, H. L.: Inheritance of Congenital Palsy in Guinea-pigs, Am. Naturalist **54**:130, 1920.

9. Wilks, S.: On Falling, Brain **9**:207, 1886.

Affective Hypertonia as a Symptom of Myotonia.—In the family of myotonic patients reported by Rosett,[10] two members had affective hypertonia.

1. Louise (Rosett's case 2) at the age of 23 was frightened on seeing her 2 year old child pulled off a chair by a neighbor's child. As she was about to move toward the children, "she suddenly experienced a wave of stiffness run through her. She felt the muscles throughout her body become tense and hard, until she could not balance herself any longer in the erect position, and she fell to the floor 'like a log of wood.' The rigidity lasted for about three minutes, during which she was perfectly conscious. The muscles relaxed in the course of another minute or two, and she was normal again." Thereafter the patient was "subject to such attacks whenever suddenly excited or surprised." When an attack occurred while she was in the sitting position, the lower limbs remained relaxed, the rigidity involving only that part of the body above the waist; when one occurred while she was standing, the entire body became rigid and she fell "like a log." Rosett witnessed an attack and verified both the rigidity and the preservation of consciousness. This, then, is a perfect case of affective hypertonia.

2. Louise's daughter, Mildred (Rosett's case 5), had this symptom: "When she is suddenly and unexpectedly pushed from behind, she falls to the floor in a rigid mass." It seems permissible here to regard unpleasant surprise as an element in the pathogenic stimulus. Though Rosett did not say so explicitly, it is clear from the context that consciousness was preserved throughout the attack.

Mildred had other symptoms of myotonia, but in Louise's case affective hypertonia was the sole neurologic symptom.

The occurrence of affective hypertonia in myotonia was known to Thomsen,[11] who wrote, on page 706 of his article: "When the subject is frightened, when unexpectedly he receives from behind a blow on his shoulder even if from a friendly hand, when he bumps his foot against an unnoticed stone, or when he unexpectedly hears a piercing sound, a sudden painful feeling darts through all his voluntary muscles, exactly as though he had got an electric shock. Every affect heightens the disposition to muscular irritability, and as fear and anger can produce the symptom, so also can joyful exaltation."

"Increased Acousticomotor Reflex."—In a discussion of certain uncommon reflex movements in infantile spastic diplegia, Oppenheim[12] described the case of a child (his case 2) who reacted to sudden noise with a brief tonic spasm of the musculature of the trunk and limbs. Thus, an attack occurred when the table was struck with a percussion hammer. Oppenheim regarded the phenomenon as "an exaggeration of simple lower reflexes" and therefore spoke of it as an "increased acousticomotor reflex." (It may be added that in the case of this child attacks occurred also when one suddenly grasped the skin of its abdomen.)

Several authors, notably Wilson,[13] have called attention to this phenomenon. Wilson recorded the case of a girl, aged 19, who had "falling attacks." "The slightest unexpected noise causes her to collapse to the ground, without unconsciousness, and apparently without any of the usual concomitants of epilepsy,

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10. Rosett, J.: A Study of Thomsen's Disease, Brain **45**:1, 1922.

11. Thomsen, J.: Tonische Krämpfe in willkürlich beweglichen Muskeln in Folge von ererbter psychischer Disposition, Arch. f. Psychiat. **6**:702, 1876.

12. Oppenheim, H.: Ueber einige bisher wenig beachtete Reflexbewegungen bei der Diplegia spastica infantilis, Monatschr. f. Psychiat. u. Neurol. **14**:241, 1903.

13. Wilson, S. A. K.: Epileptic Variants, in Modern Problems of Neurology, London, Edward Arnold & Co., 1928.

major or minor. So sudden is the attack that she is unable to save herself and has sustained bruises several times. Up to the time of her coming under my observation she has had no epileptic fit. Somatic examination is negative." Wilson did not specify the condition of the muscle tone during the attack. He reported also the case of a young man with "reflex Jacksonian epilepsy," in which the fits "commence in the right hand and are immediately preceded by a sensory aura of violent tingling in the fingers. This aura and the subsequent fit never arise 'spontaneously' but always as a sequence to a sudden extrinsic stimulus of any kind provided it is sufficient to startle him. As a single instance, a horse slipping in the street near him, with clattering feet, sent him off in a fit." The account does not say whether at any time during the fit consciousness was lost.

Keller [14] found in some children with spastic diplegia that a single handclap behind their back "sufficed to cause sitting children nearly to fall to the floor by virtue of a powerful shudder. Still more astonishing was this phenomenon in a 50 year old man, who was in an absolutely akinetic state of parkinsonism and who, when quietly accosted, . . .started (*zuckte zusammen*) so iolently . . . that this stood out in sharpest contrast with his lack of spontaneous movement." In these instances the context permits one to infer that consciousness was preserved.

Kennedy,[15] on page 605 of his article, described the case of a young man subject to "instant falling to the ground on hearing a sudden sound—a horse pawing the ground in a quiet street, a boy whistling behind him, would be enough to produce a cramp in the left leg and a quick fall in which he was always bruised. He denied any loss of consciousness, and certainly to onlookers gave, for a long period, no evidence of such. However, after two years of these events, frequently repeated, he had a major convulsion which came on after the slamming of a door and was preceded, as were the other attacks, by a feeling of a cramp in the leg. These larger seizures did not entirely replace the fallings after sudden sounds." It would appear from this account that after the onset of major convulsions the patient continued to have two kinds of attack—falling attacks, with apparent preservation of consciousness, precipitated by sudden noises, and major epileptic attacks.

The spasms of tetanus are sometimes induced by sudden noise (Conner).[16]

It is of historical interest that Charles Bell [17] was aware of cases in which the patient fell in response to excitement and sudden noise. "Thus a gentleman, capable of great bodily exertion, on going to hand a lady to the dining-room, will stagger like a drunken man; and in the streets any sudden noise, or occasion of getting quickly out of the way, will cause him to fall down." Bell made no reference to the condition of the muscles in such cases.

Miscellaneous Clinical Observations.—Keller [14] described the case of a girl, aged 12, who had attacks precipitated by excitement, as when she was censured or praised or anticipated a gift. Keller observed several attacks, in which the child became rigid, assumed a ballet-like pose, on tiptoe, with opisthotonos and abducted arms, and then fell. She often fell hard enough to injure herself. There

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14. Keller, K.: Sturzanfälle beim Kinde infolge affektiver Muskeltonuserhöhung, Deutsche Ztschr. f. Nervenh. **112**:140, 1930.

15. Kennedy, F.: Clinical Convulsions, Am. J. Psychiat. **11**:601, 1932.

16. Conner, P. S.: Tetanus, in Pepper, W.: A System of Practical Medicine, Philadelphia, Lea Brothers & Co., 1886, vol. 5, p. 550.

17. Bell, C.: The Nervous System of the Human Body, London, Longman, Rees, Orme, Brown and Green, 1830, appendix, p. 164.

were no clonic movements and no demonstrable loss of consciousness. Complete recovery always occurred after a second or two, the hypertonia disappearing during the moment she was falling. Examination showed choreiform unrest, bilateral pes equinovarus, atrophy of the muscles of the right calf and absence of associated arm movements on walking.

Spiller [18] reported two cases of obscure disease of the brain in which there were symptoms of "subcortical epilepsy." In his case 2, the patient had attacks of localized tonic spasm, lasting the better part of a minute, some of which occurred apparently spontaneously while others bore some relation to emotion. Thus, "attacks were more frequent when the patient was emotionally disturbed" (page 176), and "if she became excited she had attacks in rapid succession" (page 178). Consciousness was not affected during these attacks (page 176).

Bechterew [19] described cases of "apoplectic hemitonia" in association with signs suggestive of a lesion of the corpus striatum. One feature of these cases was the occurrence of tonic spasms, spontaneously and also in response to emotion. Thus, in regard to case 2 in his 1927 paper, Bechterew said that the "least emotion" produced an attack; "a glance at the patient suffices immediately to increase the tension of the muscles mentioned." In a case reported by Spiller, and cited in full by Molitch,[20] tonic spasms were "increased by excitement."

Vincent and Chavanny [21] reported a case of encephalitic parkinsonism in which there were attacks of tonic spasm provoked by cold, fatigue and emotion.

Tinel, Baruk and Lamache [22] reported a case in which there were attacks of decerebrate rigidity lasting from fifteen minutes to sixteen hours. Attacks were provoked by all kinds of emotion, especially anger, as well as by hyperventilation and by the injection of pilocarpine. While the patient asserted that during the attacks she was unconscious, the authors were inclined to disbelieve this.

For reasons that will become apparent later, I make special mention of the fact that hypertonia induced by *laughter* occurs very rarely. The only case I know of in which this occurred, apparently without impairment of consciousness, is one reported by Ziegler,[23] who wrote: "At times when he [the patient] wanted to laugh he could not do so because the muscles of his body would become stiff and prevented laughing." The patient never fell during an attack. Kennedy,[15] on page 603 of his paper, described a case which may be mentioned in this connection. The patient, a young man, "for some years had suffered from a sudden giving way of his legs on laughing. . . . One morning during rounds he was

18. Spiller, W. G.: Subcortical Epilepsy, Brain **50**:171, 1927.

19. von Bechterew, W.: Hemitonia apoplectica, Deutsche Ztschr. f. Nervenh. **15**:437, 1899; Apoplektische Hemitonie (Hemitonia apoplectica) als eine wahrscheinliche Form der akuten Striatumläsionen, Ztschr. f. d. ges. Neurol. u. Psychiat. **110**:695, 1927.

20. Molitch, M.: Hemihypertonia Postapoplectica, J. Nerv. & Ment. Dis. **76**: 25 (July) 1932.

21. Vincent, C., and Chavanny, J.: Syndrome parkinsonien post-encéphalitique avec crises de rigidité, Presse méd. **32**:507 (June 7) 1924.

22. Tinel, J.; Baruk, H., and Lamache, A.: Crises de catalepsie hystérique et rigidité décérébrée, Bull. et mém. Soc. méd. d. hôp. de Paris **52**:1421 (Oct. 19) 1928.

23. Ziegler, L. H.: Narcolepsy After Severe Pneumonia, M. Clin. North America **13**:1373, 1930.

sitting on the edge of the bed . . . and was made to laugh out loud. . . . Immediately, his hands were thrust out in tonic spasm, the face was tonically convulsed and cyanosed and he slid off the bed to the floor. During his fall the pupils were enlarged and fixed. He at once recovered and said he had not been unconscious. However, the fit was so brief that we could not disprove this statement though I most strongly doubt its correctness."

Experimental Observations.—Jacobson [23a] demonstrated, with the aid of suitable apparatus, the contractions of trunk muscles which occur when one "starts" in response to sudden loud noise. Löwenstein,[24] in two cases of late encephalitis and one of myoclonus epilepsy, subjected the patient to pain and fright and succeeded thereby in provoking hypertonia, the patient falling. Paskind,[25] investigating the influence of laughter and frowning in fifty healthy subjects, found that in forty-eight there was a decrease of muscle tone during laughter, and in two an increase. In thirty-nine subjects there was an increase during frowning, in eight a decrease and in three no change.

Epileptic Attacks Precipitated by Emotion.—Though this paper deals primarily with attacks in which there is no loss of consciousness, brief allusion may be made to the well known fact that typical major epileptic attacks are sometimes precipitated by surprise and other emotions. Foerster [26] mentioned a case in which epileptic attacks "could be provoked with experimental promptness by letting an object fall on the floor, or by the noise of a passing tramcar." Cobb [27] related the case of a boy who had an epileptic fit when barked at by a dog in Cobb's laboratory.

In some cases the evidence as to loss of consciousness is suggestive but not conclusive. Cooper [28] reported a case in which there were tonic spasms, during which consciousness was "probably" disturbed "to some degree." The pupils, during the attack, were dilated and did not react to light. Attacks sometimes occurred as a result of fright and surprise, as when there was an unexpected sharp noise, or when the patient's ear was suddenly flicked or his face slapped.

Three remarkable cases, reported, respectively, by Ogle,[29] Dunsmure [30] and Hughlings Jackson,[31] may be cited together. Their common feature was that attacks were produced by touching certain parts of the body. In Ogle's patient

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23a. Jacobson, E.: Response to a Sudden Unexpected Stimulus, J. Exper. Psychol. **9**:19, 1926.

24. Löwenstein, O.: Ueber affektbedingte Tonusschwankungen, Arch. f. Psychiat. **85**:276, 1928.

25. Paskind, H. A.: Effect of Laughter on Muscle Tone, Arch. Neurol. & Psychiat. **28**:623 (Sept.) 1932.

26. Foerster, O.: The Cerebral Cortex in Man, Lancet **2**:309 (Aug. 8) 1931.

27. Cobb, S.: Causes of Epilepsy, Arch. Neurol. & Psychiat. **27**:1245 (May) 1932.

28. Cooper, M. J.: Tonic Epileptic Attacks Precipitated by Fright or Surprise, Arch. Neurol. & Psychiat. **30**:462 (Aug.) 1933.

29. Ogle, J. W.: Case of Epilepsy Presenting Features of Unusual Interest, Lancet **1**:615 and 651, 1874.

30. Dunsmure, J.: Note of a Case of Temporary Loss of Voluntary Power, Produced by a Touch on the Head, Edinburgh M. J. **20**:319, 1874.

31. Jackson, J. Hughlings: On a Case of Fits Resembling Those Artificially Produced in Guinea-pigs, Proc. M. Soc. London **10**:78, 1887.

the slightest touch on parts of the left arm or left side of the neck sometimes produced a tonic spasm involving chiefly the left side, during which consciousness "was but slightly interfered with." In both Dunsmure's case and Jackson's case it was emphasized that the touch must occur unexpectedly. In Dunsmure's case a touch on any part of the head produced an attack; in Jackson's case, a touch on any part of the head or face. In both cases there was some hypertonia. With respect to the state of consciousness there was some doubt; Jackson, in a later article,[32] said, in comparing the two cases: "It was not certain that in either case there was loss of consciousness in the seizure. I thought there was in my patient's attacks and Dr. Dunsmure thinks there may have been in his patient's attacks." Both patients also had major epileptic fits.

REPORT OF THREE PERSONALLY OBSERVED CASES

CASE 1.—*A woman, aged 59, who reached puberty at 16, from the ages of 11 to 17 had numerous brief attacks of inability to move, accompanied by a feeling of stiffness, occurring in response to anger, resentment, shame and other painful emotions. After 17 she had only one attack, at 43.*

This intelligent patient, a widow, was admitted to the Harrisburg State Hospital on Nov. 13, 1931, in a paranoid state which had begun the preceding summer. In all matters unrelated to her paranoid ideas she conversed sensibly. Her memory was excellent.

Affective Hypertonia.—From her twelfth to her eighteenth year the patient had a number of brief attacks of stiffness and inability to move, which were induced by certain painful emotions. She recalled the following examples: 1. The first episode occurred at 11 years of age. A group of children had gathered in her house ready to leave on a sleighing party. The patient, like the others, was bundled up, ready to go. Probably as a result of excitement, she urinated involuntarily. Chagrined, and ridiculed by a maid servant, she made her way to a toilet on the ground floor. Having removed some of her wet garments she was about to leave for her room upstairs for some dry clothes. She dreaded passing her playmates with the telltale wet garments in her hands. Just as she was about to open the door of the toilet, as she stated, "I found for an instant or two that I couldn't go. My feet were leaden, I couldn't take the first step to go. . . . I was [however] able to move my arms, because I remember tucking my wet leggings under my arm, so that the children wouldn't see them."

2. At 14, at the funeral of an uncle, she saw her bereaved aunt. "I saw my aunt's distressed face. My pity for her seemed to give me a chill, *there seemed to be a stiffening of my body—a tenseness*—a feeling as though the spine refuses to make the feet move. I stood still on the spot."

3. At 14, an attack was precipitated by a situation provocative of sudden chagrin, occurring as the patient stood at the door, her hand on the door-knob. At that moment, "I had one of those nervous chills. I was tense." There was a pattern in the door-knob; she held it so tight that the pattern was impressed on her palm. "I wanted to close the door . . . but *I couldn't.*"

Similar attacks occurred when her hated stepmother shamed her openly and once when her father, whom she adored, disappointed her by failing to keep a promise.

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32. Jackson, J. Hughlings: Fits Following Touching the Head, Lancet **1**:274, 1895.

In every case the attack lasted only a few seconds. *Only once did the patient lose consciousness.* Shortly after the onset of puberty (at 16), on the first day of a menstrual period, she was scolded by her stepmother in the presence of friends. She had a "nervous chill" and lost consciousness for a short period. When she had regained consciousness there was no muscular soreness, nor had she lost control of her sphincters.

After the age of 17, the patient had only one attack. This was when she was 43. Her son was standing on the stairs chatting with his mother, who was a few feet above him. Playfully she tapped him, causing him to lose his balance, and he fell seven steps. "I simply stood *rooted to the spot.* I kept saying, 'Oh, son, I didn't mean to do it. I know you're dead, but I didn't mean to do it.' I wanted to go down and help him, but *I couldn't move. From the waist down I felt paralyzed: I seemed to have no power over my feet and legs.* I was so horrified to think I had *pushed* him down the steps." In a few moments he got up and laughed, uninjured, whereupon immediately she regained the use of her legs.

It is noteworthy that the shock of coming home and discovering her beloved and only son dead of a self-inflicted bullet wound (1927) produced no attack.

Laughter never produced an attack. The patient never had morbid somnolence or cataplexy. Neurologic examination gave negative results. General physical examination revealed nothing but moderate arteriosclerosis, peripheral and retinal.

Comment.—It is noteworthy that the hypertonia involved chiefly the lower limbs: "a feeling as though the spine refuses to make the feet move." In the third episode cited, the upper limbs also were affected.

CASE 2.—*A woman, at 20 had a bromide hallucinosis which lasted four months and disappeared one month after discontinuance of the bromides. During the hallucinosis she had numerous brief attacks of stiffness of the hands and inability to flex or separate the fingers, occurring in response to sudden fright or unpleasant shock.*

This patient's bromide hallucinosis has been fully described in a previous article,[33] in which she is listed as case 8. The hallucinosis began in November 1931 and disappeared at the end of February 1932.

Affective Hypertonia.—In giving a retrospective account of the hallucinosis (of which she had a clear recollection) the patient revealed that during the psychosis she had had many brief attacks of hypertonia induced by sudden unpleasant emotions. The hypertonia was, with rare exceptions, limited to both hands. The position of the wrists was midway between flexion and extension and midway between pronation and supination. The fingers were in extension and felt stiff. She was able neither to flex nor to separate them. "They seemed all stuck together." On several occasions she forced her fingers apart by prying them against some fixed object, but "when I got them apart they just stayed where they were." The hands felt numb and cold, up to a point several centimeters above the wrist. On a few occasions, in addition to the hands, the left leg also felt numb and stiff, up to a point about 5 cm. below the knee. *There never was loss of consciousness.* In each instance the attack cleared up in not more than two or three minutes, after which she was able to move as freely as ever.

The patient recalled the following actual instances: 1. The first attack occurred at the end of November 1931, in the fluoroscopy room of a hospital. The room was pitch-dark, and the patient was in a state of uneasy anticipation. Presently

33. Levin, M.: Bromide Delirium and Other Bromide Psychoses, Am. J. Psychiat. **12**:1125, 1933.

the nurse pressed a lever, producing a "buzz," which had a gruesome startling effect on the patient. "I was frightened and hollered, and my fingers got stiff, they all went together."

2. She was given a cold wet pack in December 1931. The first contact with the cold sheet induced a typical attack of hypertonia.

3. The "voice of the devil" (which frequently came to her during the hallucinosis) told her that her mother was going to die soon. This frightened her, and an attack followed.

4. The last attack occurred on Feb. 13, 1932, two days before admission to the Harrisburg State Hospital. She was riding in the back seat of an automobile. Unexpectedly a motorcycle policeman, going in the same direction, overtook and passed them, a loud roar issuing from his machine. "It scared and upset me," and an attack followed.

Remarkably, her frequent hallucinations of animals never evoked an attack, even though they frightened her much more severely than the stimuli already cited. She expressed the opinion that the *suddenness* of the fright determined its effectiveness in precipitating an attack. The imaginary animals generally appeared first at a distance and then came nearer, so that her feeling of fright was not a sudden one. On the other hand, the buzz in the fluoroscopy room produced a sudden fright or shock, as did also the first contact with the cold sheet and the unexpected roar of the motorcycle.

Laughter never produced any symptoms. The patient never had morbid somnolence.

On March 10, 1932 (about ten days after the termination of the hallucinosis), I attempted to produce an attack of hypertonia. I succeeded in inducing a sudden and severe fright, but no attack of hypertonia followed.

Comment.—The attacks of affective hypertonia began about two weeks after the onset of the hallucinosis, while the patient was still taking bromides. They continued for about three months, ceasing two weeks after the discontinuance of the bromides and two weeks before the termination of the hallucinosis.

The distribution of the hypertonia differs from that in case 1.

CASE 3.—*A woman, aged 21, at 17 began to have an inconstant tremor of the trunk and upper limbs, which was present also during sleep. At 20 she began to have attacks of "sleep paralysis," and at 21 attacks of cataplexy. At 21 she also began to have attacks of hypertonia precipitated by fright, surprise and anger; attacks of hypertonia occurred also on awakening from bad dreams.*

In a previous article [34] I reported the case of a young woman who had attacks of "sleep paralysis," of cataplexy and of affective hypertonia. The details already published I shall not repeat here, but I shall amplify certain points to which only passing reference was made in the previous report. The attacks of affective hypertonia began in July 1932. They will be separated into those which occurred during the day and those on awakening.

Diurnal Attacks of Affective Hypertonia.—The following are examples of severe attacks: 1. In July 1932, the patient while walking in her garden came very close to a snake before seeing it. "I was so near it that I almost tramped on it. It wriggled, and that's how I came to see it. I threw my arms up and then they dropped down, and I was *so stiff I* [literally] *couldn't move.*" She

34. Levin, M.: The Pathogenesis of Narcolepsy, with a Consideration of Sleep-Paralysis and Localized Sleep, J. Neurol. & Psychopath. **14**:1, 1933.

remained standing for what seemed several minutes, during which she was fully conscious but rigid and absolutely paralyzed. Her arms were adducted and extended at the elbow; when she described the attack to me, several weeks later, she no longer remembered whether the hands had been in pronation. Finally, members of the family, a short distance away, noticing her plight, called to her. "When they called to me, it seemed to relieve the fear—I knew I wasn't alone. The moment they called to me I was able to move."

2. One afternoon in August 1932 the patient was walking in the garden with her sister. Wearing socks, she suddenly felt and immediately saw a large woolly caterpillar on her left leg, on the edge of the sock. "I screamed, and then I began to feel funny. *I got stiff all over,* I couldn't move." The sister, knowing the patient abhorred caterpillars, brushed it away, but the patient continued to be stiff and paralyzed for several minutes, after which she suddenly was able to move again.

In addition to the severe attacks, the patient had milder attacks when angry or annoyed. "When I get real cross at some one, I get stiff all over, so stiff that I can't talk. I *try* to talk, but can't. I just stand there, and after a little while I'm able to talk again."

Unexpected sharp noises were especially capable of frightening the patient. On several occasions noises frightened her even though she expected them. Thus, she once stood about 4 feet away from a man who was shooting birds. She expected the shot, yet when it came she was "stiff and paralyzed" for a fraction of a minute.

On rare occasions, hypertonia occurred with no apparent precipitating cause. Thus, in the diary which she kept at my request there is this notation made on April 11, 1933: "Just got stiff. Can't remember any cause—was lying on the bed reading."

In none of the attacks of hypertonia did the patient lose consciousness, nor did she fall or lose control of her sphincters. (By contrast, in the attacks of cataplexy she sometimes fell.)

Postdormitial Affective Hypertonia.—The patient had many bad dreams, from which she sometimes awoke feeling temporarily stiff and paralyzed. The following examples will suffice:

1. In January 1933 she received news that her house had burned down to the ground. (Her immediate reaction to this news will be described later.) Several days later, in a dream, she saw her house in flames. "I woke up and was scared and stiff all over. For a minute I couldn't move. At last, when I was able to move, I was so nervous and shaky I could hardly keep still."

2. In February 1933 she dreamed that she was lost in a large building. "I tried to jump out the window. Then I awoke, stiff, and couldn't speak or move for several minutes."

Cataplexy on Unpleasant Emotion.—The patient's cataplexy occurred most often during laughing, but sometimes it occurred during unpleasant emotion, as when she was startled by the dog barking, by the wind slamming the door or by some one silently entering the room. When the news came to her that her house had burned down she had a cataplectic attack; she received the news while sitting, talking over the telephone; during the attack she felt "limber" and for a minute was unable to talk, but she did not fall or drop the receiver. (It is remarkable that several days later, when she dreamed of the fire, she awoke with hypertonia.)

Attacks of hypotonia also occurred sometimes on awakening from a bad dream; e.g., in March 1933, she "awoke after dreaming I was in an Indian cave, where there were many wild animals and snakes." She was "limber."

In one instance unpleasant emotion led to first hypertonia and then hypotonia. She dreamed that some one was talking to her and awoke with the uneasy feeling that someone was in the room. For a short time she was "stiff with fear" and after that "limber and cold." Hypotonia followed by hypertonia never occurred.

While hypotonia sometimes occurred during unpleasant emotion, there was no instance in which hypertonia occurred during pleasant emotion.

I witnessed none of the patient's seizures.

Comment.—I know of but one other case in which postdormitial hypertonia occurred—the case of a diabetic patient reported by Wuth.[35] The patient had reactions to insulin accompanied by mental symptoms. He had a postdormitial attack, of which he gave the following account: "Yesterday evening, as usual, I took an injection at 8 o'clock, after which I ate with a friend, which may perhaps indicate that I did not take care to eat a sufficient amount of carbohydrate. Toward 11 o'clock I went to bed, feeling perfectly normal, and awoke at 3 o'clock almost completely paralyzed. . . . I could scarcely move my hands, and my body was almost completely stiff (*steif*). But, remarkably, I was perfectly conscious, and I knew immediately on waking what the trouble was and what I must do. With the greatest difficulty I succeeded in reaching for the piece of chocolate which I always keep at my bedside. Even after eating it, the tightness (*Gebundenheit*) of my body was such that I could get to the door only by supporting myself on the bed and chair; for I understood my condition so well that I reflected it was necessary to unlock the door, so that in case of need someone could come to me." The duration of the attack was not given. The patient fell asleep again and "awoke this morning feeling quite normal, except for a slight heaviness in the limbs."

COMMENT

From the cases cited in this paper it will be seen that with striking regularity the emotions which precipitate hypertonia are distinctly unpleasant. Thus, hypertonia is precipitated by sudden sharp noise; by fright, as when the patient sees a snake; by shock, as at the first moment of contact with a cold pack, or when the patient sees her child being pulled off a chair; by censure and embarrassment, and in one case (my case 1) by pity. In response to careful questioning my three patients recalled all the episodes they could; in each instance the attack came on as a result of some unpleasant emotion. There were only two cases in which hypertonia was provoked by pleasant emotion: Ziegler's case, in which laughing caused the patient to feel stiff, and Keller's case, in which attacks occurred not only when the patient was censured but when she was praised or anticipated a gift. (See also Thomsen's statement that "joyful exaltation" may produce muscular spasm in patients with myotonia.)

In striking contrast with the fact that hypertonia occurs (with rare exceptions) in response to unpleasant emotion, cataplexy occurs characteristically in response to pleasant emotion. In the vast majority of cases the common occurrence of cataplexy is during hearty laughter. In those cases in which cataplexy occurs also in situations other than laughter, as often as not the situation is one of pleasurable excitement (receiving a good hand at cards, unexpectedly meeting

35. Wuth, O.: Ueber psychische Krankheitserscheinungen bei Hypoglykämie, Monatschr. f. Psychiat. u. Neurol. **73**:129, 1929.

an old friend on the street, sexual orgasm, etc.). In only a small minority of cases does cataplexy occur during unpleasant emotion exclusively. In a group of sixty-six cases of narcolepsy,[36] representing all I found in the literature up to 1929, there were only five in which cataplexy occurred during unpleasant emotion and not during laughter.

In view of this contrast in the clinical occurrence of affective hypertonia and hypotonia, one is not surprised to read that Paskind found experimentally in healthy people that during laughter there is usually a decrease in muscle tone, while during frowning there is usually an increase. The contrast finds expression in everyday language when people say they are "weak with laughter" but, on the other hand, "scared stiff." Rothfeld[37] brought out the contrast vividly when he compared the appearance of a man following a hearse with that of a boy marching behind a military band: the former is bowed with grief, his face and body are comparatively rigid and there is restriction of the associated arm movements on walking (an "akinetic-hypertonic" picture); the latter carries himself erect, swings his arms briskly and displays lively facial mimicry (a "hyperkinetic-hypotonic" picture).

It seems permissible to conclude that paroxysmal hypertonia occurring during unpleasant emotion and cataplexy occurring during pleasant emotion represent exaggerations of reactions found in healthy people.

The conclusions up to this point seem amply warranted by clinical and experimental data. It is when one comes to the pathogenesis of affective hypertonia that one is on uncertain ground. One may say that there is a reflex mechanism whereby stimuli such as fear and surprise cause an increase of muscle tone. In mature healthy people this reflex under ordinary circumstances appears only in rudimentary form, being presumably inhibited by higher centers. It therefore seems possible that affective hypertonia may appear in either of two ways: (1) through increased irritability of the reflex arc in question, in a way comparable to the increased irritability of spinal arcs in strychnine poisoning; (2) through dissolution of the higher inhibitory centers, this being comparable to the increase in the knee jerk in dementia paralytica without tabes. One must therefore ask two questions:

1. What is the reflex arc by means of which muscle tone is increased in response to the proper stimuli? The constitution of this arc is obviously unknown. One may say only that the arc is probably extraordinarily complicated and that it probably includes portions of the thalamus and the corpus striatum.

2. What are the higher pathways whose interruption permits the unchecked action of the reflex arc mentioned in the first question? This question is equally difficult to answer. It is noteworthy that in some cases the posture during affective hypertonia is that seen in decerebrate rigidity. The best example is the case of the "nervous goats." During their attacks the goats maintain the quadrupedal standing posture; it is permissible to conclude that these attacks represent a transient decerebrate rigidity. This conclusion possibly applies also to my case 3, in which the patient during severe attacks stood stiff, her arms rigidly adducted and extended at the elbow. In another case (Keller) the posture was typical of decerebrate rigidity in so far as there were opisthotonos and extensor rigidity of

36. Levin, M.: Narcolepsy (Gélineau's Syndrome) and Other Varieties of Morbid Somnolence, Arch. Neurol. & Psychiat. **22**:1172, 1929.

37. Rothfeld, J.: Affektiver Tonus- und Bewusstseinsverlust beim Lachen und Orgasmus (Gelo- und Orgasmolepsia), Ztschr. f. d. ges. Neurol. u. Psychiat. **115**: 516, 1928.

the legs, but atypical in that the arms were abducted. The case reported by Tinel, Baruk and Lamache was one of attacks of decerebrate rigidity provoked by emotion and other means; it differs from the other cases cited in this paper in that the attacks lasted, not a few minutes but from one-quarter to sixteen hours. In view of these observations one may entertain the hypothesis that the higher pathways mentioned in the first sentence of this paragraph have some relation to the pathways that inhibit decerebrate rigidity.

The reader will already have recognized that in many cases the posture is not that of decerebrate rigidity. This is seen particularly in my case 2, in which the patient noticed that during the attacks her wrists were midway between flexion and extension and midway between pronation and supination, her fingers fully extended. It is therefore apparent that the statement contained in the concluding sentence of the last paragraph is not universally applicable; at most it may prove true in some cases.

Two puzzling facts must be mentioned: 1. In two cases affective stimuli produced first hypertonia and a few moments later hypotonia. One is the case reported by Redlich [38] on page 140 of his paper; in this case, at the beginning of a cataplectic attack there was "a sort of stiffness of the arms and legs." The other is my case 3; the patient once awoke from a dream "stiff with fear" and, shortly after that, was "limber." 2. In the case of the "nervous goats" it was observed that when they have had an attack they cannot have another for twenty or thirty minutes, no matter how badly one may frighten them. A similar observation was made in the case reported by Ogle, who wrote: "In order that an attack should be induced a second time, it was necessary that an hour or two should have elapsed after the first one, as if to permit of an accumulation of force."

It is of interest to consider certain tentative conclusions that may be drawn regarding etiology. The "nervous goats" probably suffer from hereditary inferiority of the higher inhibitory pathways. In my case 2, affective hypertonia occurred only during a severe bromide intoxication. Since bromides are cortical poisons, they probably caused temporary paralysis of the higher inhibitory pathways. In the case of the sheep studied in Patagonia by Jones and Arnold, the symptom occurred only after the animals had eaten a certain toxic grass. The nature of the poison contained in this grass is not known. Is it a cortical poison or, like strychnine, an irritant to lower reflex arcs? If the former, one will have to assume that the poison causes affective hypertonia by paralyzing the higher inhibitory pathways; if the latter, one will have to assume that it acts by heightening the irritability of certain lower arcs. It is noteworthy that in their first year of life sheep are more susceptible to this poison than later. This may mean that the higher pathways, being in lambs relatively underdeveloped, are (on the first assumption) more susceptible to the paralyzing effect of the poison or (on the second assumption) less capable of keeping in check the unduly irritated lower arcs.

Affective hypertonia is obviously only a symptom and never a disease.

SUMMARY

Cases are described in which emotional stimuli produce a state in which the patient is paralyzed and feels stiff; the muscles on palpation are hard; consciousness is not impaired; the patient usually recovers in not more than a few minutes. This is the full-fledged form of the symptom. There is also an incomplete form, in

38. Redlich, E.: Epilegomena zur Narkolepsiefrage, Ztschr. f. d. ges. Neurol. u. Psychiat. **136**:128, 1931.

which there is generalized hypertonia lasting only a moment or hypertonia localized in one or more limbs. The symptom may be called paroxysmal affective hypertonia. The commonest effective stimuli are sudden sharp noise, unpleasant surprise, fright and shock. Other stimuli are censure, embarrassment and pity. Very exceptionally attacks are produced by pleasant stimuli.

Affective hypertonia may be contrasted with affective hypotonia, or cataplexy. The two symptoms have these features in common: The patient is conscious and in severe instances completely paralyzed; recovery occurs in a few minutes. They differ in the fact that muscle tone is increased in the one and abolished in the other and in the fact that hypertonia is characteristically evoked by unpleasant and cataplexy by pleasant stimuli. This contrast in the nature of the effective stimulus accords with Paskind's experimental demonstration in healthy people that during laughter there is usually a decrease and during frowning usually an increase in muscle tone. It accords also with common experience as shown in everyday language: People say they are "weak with laughter" but, on the other hand, "scared stiff."

One may postulate a reflex mechanism whereby stimuli such as fear and surprise cause an increase of muscle tone. In mature healthy people this reflex under ordinary circumstances appears only in rudimentary form, being presumably inhibited by higher pathways. If this is true, affective hypertonia may appear in either of two ways: (1) through increased irritability of the lower reflex arc, due to poisons which have an effect similar to that of strychnine, and (2) through interruption of the higher inhibitory pathways. Some clinical data are in keeping with these assumptions, but it is emphasized that nothing is known with certainty concerning the pathogenesis of affective hypertonia.

PNEUMOCRANIUM IN THE TREATMENT OF TRAUMATIC HEADACHE, DIZZINESS AND CHANGE OF CHARACTER

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Headache and dizziness have always been recognized as common sequelae of cerebral concussion and trauma. In many cases these distressing symptoms persist even after the most conservative treatment in the acute stage of concussion. There is, however, another important sequel of cerebral concussion which thus far has not received the attention it deserves. This sequel is change in character.

In many cases change in character has been observed following cerebral trauma, but its true significance has not been appreciated because the majority of cases showing alterations in personality following head injury have been classified as cases of traumatic neurosis. This diagnosis presupposes that the symptoms are purely functional, and the fact that many persons with posttraumatic symptoms either apply for or receive compensation has usually inclined the clinician toward this diagnosis.

It was not until the development of the technic of encephalography that the full significance of the sequelae of cerebral concussion was appreciated. The encephalogram not only proved to be a valuable aid in the diagnosis and localization of intracranial lesions but also revealed that the syndrome of headache, dizziness and change in character is of organic rather than of functional origin.

Penfield[1] was the first to observe the therapeutic value of lumbar insufflation of air in posttraumatic cases. In 1927, he reported a series of seven cases, all with intense headache and dizziness following cerebral concussion or fracture of the skull, which were either entirely relieved or definitely improved by this procedure.

On the basis of this work about one hundred patients with posttraumatic cases of residual headache, dizziness and changes in character following cerebral concussion have been treated with satisfactory results. At first the aim was to relieve or try to relieve these patients of the violent headaches and dizziness. Later I was pleased to discover that many changes in character often exhibited by these patients either partially or entirely disappeared, in some for a few months, in others for several years.

The changes in character frequently observed following cerebral concussion are extreme irritability, inability to endure noise without emotional upset, marked restlessness, hyperactivity, emotional instability and distinctly antisocial behavior. The antisocial behavior ranges in severity from petty thievery to burglary, assault and

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Read at a meeting of the Philadelphia Neurological Society, April 27, 1934.

1. Penfield, W.: Chronic Meningeal Post-Traumatic Headache, Surg., Gynec. & Obst. **45**:747 (Dec.) 1927.

battery, serious sex delinquencies and even murderous attacks. Many of these cases were called to my attention chiefly on account of the disturbances of behavior, the delinquencies having been severe enough to warrant the arrest of the patient.

Unfortunately, owing to the fact that many of the patients have moved from their former residences or have otherwise dropped from view, thus far only fifty cases have been adequately followed. Only cases in which the follow-up has been complete will be reported.

In all the cases the lumbar insufflation of air was performed according to the usual technic, with the patient in the sitting position. A lumbar puncture needle with a three-way stop-cock was used. Three or four minutes were allowed to elapse after the manometer was attached to the needle in order that the most accurate reading possible of the pressure might be obtained. Spinal fluid was drawn off in a syringe in quantities of 10 cc. at a time, and after each withdrawal of fluid 10 cc. of air was injected. The patient's head was rotated from side to side in order to drain away the maximum amount of cerebrospinal fluid. Determinations of pressure were made following each withdrawal of 30 cc. of fluid and injection of 30 cc. of air. Toward the end of the procedure it was usually possible to obtain a terminal pressure of from 8 to 12 mm. of mercury by juggling the amount of fluid withdrawn and the amount of air introduced. The amount of fluid ranged from 80 to 178 cc., depending largely on the size of the head, the amount of pressure and the patient's condition. In addition to a complete physical and neurologic examination, an examination of the eyegrounds was made by an ophthalmologist in each case before the lumbar insufflation of air was performed. After the encephalogram the patient was kept in bed with the head elevated until the headache disappeared. The duration of headache after insufflation with air is usually from twelve hours to one week. The average duration of headache is about two days.

It is not my purpose to discuss the pathologic changes underlying these posttraumatic symptoms. The encephalograms in my cases conform with those of Penfield, which were not consistent. Some plates revealed no alteration from what is believed to be normal; others showed small or large areas of cortical atrophy. There was a distortion or dilatation of the ventricles in some, and still others showed areas of arachnitis, probably the cystic arachnitis serosa described by Foerster.[2] However, Grant[3] pointed out that the roentgenographic diagnosis "arachnitis" does not necessarily indicate the presence of inflammatory adhesions, but may mean merely failure of drainage of cerebrospinal fluid or lack of air in certain regions, the reason for which cannot be pathologically demonstrated.

The most constant finding during the procedure is an increase in the cerebrospinal fluid pressure. In a series of control cases readings of cerebrospinal fluid pressure with the patient in the sitting position ranged from 10 to 20 mm. of mercury, with an average of 15 mm. In my series of posttraumatic cases with definite symptoms, the pressure ranged from 10 to 48 mm. of mercury; in 8 per cent of the cases it was under 20, in 32 per cent between 20 and 30, in 48 per cent, between 30 and 40, and in 12 per cent, over 40 mm. of mercury.

I am loath to claim that this increase in intracranial tension might be responsible for the production of the symptoms, but in four cases of recurrence of

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2. Foerster, O.: Encephalographische Erfahrungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **94**:515, 1924.

3. Grant, F. C.: Ventriculography and Encephalography, Arch. Neurol. & Psychiat. **22**:1310 (June) 1932.

symptoms after encephalography I observed that the intracranial tension was again high and that reduction of this tension produced relief of the symptoms. These four patients requested that the pneumocranium be repeated because of the relief they experienced from the first insufflation of air. One patient had four lumbar insufflations of air with progressive improvement. Perhaps the negative results obtained by some who have employed this method of treatment was due to the return of increased intracranial tension following the pneumocranium. There should be no hesitation in repeating the procedure two or even three times if satisfactory results are not obtained on the first attempt.

On the whole this method of treatment has proved to be satisfactory in the majority of cases. Headache was completely relieved in forty-one of the forty-six patients who complained of this symptom. Dizziness was a prominent feature in forty-six, and of these, forty-three were relieved. On the other hand the results in traumatic epilepsy are not significant. Only ten patients presenting this symptom were treated, and from this small series no satisfactory conclusions can be

TABLE 1.—*Therapeutic Results*

	Number of Cases	Per Cent
Headache	46	
Completely relieved	41	89.13
Unimproved	5	10.87
Dizziness	46	
Completely relieved	43	93.48
Unimproved	3	6.52
Convulsions	10	
Completely relieved	2	20
Improved	6	60
Unimproved	2	20
Changes of character	43	
Normally adjusted	21	48.84
Improved	16	37.21
Unimproved	6	13.95

drawn. Two have had no convulsions since lumbar insufflation of air was performed. One patient has been free from convulsions for two years, the other for ten months. Six patients have had less frequent attacks since they were treated, and two are unimproved.

The results obtained in posttraumatic change in character have been gratifying not only from the medical but also from the social standpoint. A large majority in this series are court cases. It is interesting that most of these persons formerly had been well adjusted; in many the personality change following the head injury was so serious that the resulting antisocial conduct led to arrest. Of the forty-three patients with change in character twenty-one were entirely relieved of the abnormal manifestations and able to resume their accustomed places in society. Sixteen are improved to such an extent that they are now able to make a fair adjustment; only six are unimproved. The possibility of the beneficial psychologic effect of constant medical supervision cannot be considered a factor in the improvement of these patients. Only the unimproved have been closely supervised. No person considered to be well is asked to report to the clinic oftener than once in six months, while many reports have come from members of the family or from insurance companies.

TABLE 2.—*Results of Pneumocranium*

Name	Age	Sex	Head Injury		Posttraumatic Symptoms			Pneumocranium					Result		
			Date	Nature	Headache	Dizziness	Changes in Character and Other Symptoms	Date	Fluid Removed, Cc.	Air Injected, Cc.	Cerebrospinal Fluid Pressure, Mm. of Mercury: Before	Cerebrospinal Fluid Pressure, Mm. of Mercury: After	Headache	Dizziness	Character
J. B.	12	M	9/ 1/30	Fracture of skull	+	+	Defective memory; steals	3/10/31	90	110	30	10	0	0	Complete recovery until 4/4/32 when skull was fractured again and headache recurred
A. D.	57	M	1915	Concussion	+	+	Violent rages; unable to work	10/18/32	133	141	33	8	0	0	No more rages, slight sensitivity to loud noises; great improvement
P. B.	47	M	10/ 6/28	Concussion	+	+	Violent rages; unable to work	11/20/28	150	150	28	6	+	+	Complete recovery for a while, recurrence of symptoms when compensation was stopped
W. B.	26	M	4/19/29	Concussion	+	+ Could not stand up	Irritable; paranoid	2/13/30	125	125	34	4	0	0	Complete recovery; working ever since
A. D.	33	F	10/10/30	Concussion	+	+	Violent rages; hysterical	2/24/31 6/ 5/31 4/11/33	130 129 121	136 141 121	30 36 28	8 12 10	+ 0 0	0 0 0	Dizziness improved; headache gone; hysteria persisting; hysterical attacks improved
F. D.	51	M	1903 1906	Concussion Fracture	+	+	Headache after 1903; paranoia, hallucinations after 1906; murderous attacks in Norristown State Hospital 1912-1916	8/24/28	100	100	40	10	0	0	Complete recovery
C. E.	35	M	6/ 2/30	Concussion	+	+	Extreme irritability; staggers and falls	1/27/31	160	161	35	14	0	0	Complete recovery except for headache in hot weather
C. F.	27	M	6/12/28	Concussion	+	+	Marked irritability; unable to work	7/13/28	125	120	..	..	0	0	Complete recovery
E. D.	14	F	.....	Concussion	+	+	Sex offenses, intelligence quotient 45	6/ 7/29	...	...	..	..	0	0	Well for 1½ years, then headaches and dizziness returned
E. G.	16	M	1921	Concussion	+	+	Steals; violent murderous attacks; chronic encephalitis	10/ 7/32	146	146	36	26	0	0	Slight improvement in behavior
A. G.	11	M	1925	Concussion	+	0	Jacksonian epilepsy; feebleminded	10/24/30	106	111	12	10	0	0	Jacksonian attacks diminished in number and severity
A. G.	12	M	1923	Concussion	0	0	Epilepsy	7/14/31	135	135	30	14	0	0	Has had one fit since encephalogram

TABLE 2.—*Results of Pneumocranium—Continued*

Name	Age	Sex	Head Injury		Posttraumatic Symptoms			Pneumocranium						Result		
											Cerebrospinal Fluid Pressure, Mm. of Mercury					
			Date	Nature	Headache	Dizziness	Changes in Character and Other Symptoms	Date	Fluid Removed, Cc.	Air Injected, Cc.	Before	After	Headache	Dizziness	Character
M. F.	18	M	1923	Concussion	+	+	Violent temper; murderous attacks; smashes furniture; chronic encephalitis	3/15/33	178	178	44	10	0	0	Quiet and well behaved for one month
C. H.	9	M	1927	Concussion	+	+	Fights, steals; pinches young children	7/29/33	92	92	32	14	0	0	Complete recovery; behavior good; doing well at school
T. H.	16	M	1925	Concussion	+	+	Twelve arrests for burglary	2/ 9/32	93	93	38	12	0	0	One theft since encephalogram; now in Huntingdon Reformatory
F. K.	33	F	1904	Concussion	+	0	Feebleminded; epileptic	10/30/31	139	144	18	12	0	0	Occasional fits
J. L.	14	M	1926	Concussion	+	+	Lies; steals; runaway; arrested for burglary	1/15/29	90	90	30	8	0	0	Working steadily; well behaved; no arrests
H. M.	11	M	1922	Concussion	+	+	Steals; restless; hyperactive	2/26/30	85	95	26	2	0	0	Well behaved
A. M.	16	M	....	Forceps delivery; head injury at birth	+	+	Runaway; steals; mentally dull	1/26/32	150	150	28	10	0	0	Behavior excellent; has not run away since receiving treatment
C. N.	10	M	1926	Concussion	+	+	Steals; "devilish"	10/26/32	99	119	22	16	0	0	Behavior good
H. P.	13	F	1923	Concussion	+	0	Incorrigible; filthy; hypersexed	4/ 2/30	115	125	32	16	0	0	Well behaved for 1 year then asked for another encephalogram; well for 6 months; now has occasional temper tantrums
								2/20/31	105	115	29	10	0	0	
C. S.	39	M	1925	Concussion	+	+	Irritable; murderous attacks on wife	11/12/29	140	140	36	10	0	0	Complete recovery
J. S.	9	M	7/ 1/29	Fracture of skull	+	+	Steals; restless; lies	8/30/30	95	95	28	8	0	0	Behavior excellent
A. W.	17	M	1921 1927	Concussion Concussion	+	+	Seven arrests for stealing since 1927	5/13/32	181	178	48	12	0	0	Behavior excellent
J. H.	14	M	....	Head injury at birth	+	+	Jacksonian epilepsy; misbehaves; one fit a month since age of 8 years	8/13/30	99	97	30	6	0	0	Since encephalogram only one fit in 2½ years; no phenobarbital for 6 months; conduct excellent
E. H.	26	M	....	Concussion	+	+	Very irritable	6/ 1/30	135	135	32	16	0	0	Still irritable; result poor except for improvement of headache and dizziness
S. W.	42	M	1924	Severe fracture of skull	+	+	Violent rages; murderous attacks on child	9/26/30	125	120	30	14	0	0	Working, compensation stopped; result fair
C. W.	13	M	1928	Concussion	+	+	Arrested five times for stealing; also chronic encephalitis	1/ 5/32	88	85	28	8	0	0	Doing well at Glen Mills School

M. Z.	13	F	1926	Concussion	+	+	Violent temper tantrums	6/16/31	66	71	36	12	0	0	Improved for a time then temper tantrums recurred; committed to Allentown State Hospital
T. Y.	17	F	1931	Concussion	+	+	Irritable; lies; steals	1/31/33	130	130	44	12	0	0	Behavior good thus far
R. D.	15	M	1925	Concussion	+	0	Irritable	8/29/32	91	118	26	9	0	0	Improved
P. B.	12	M	1925	Concussion	0	0	Epilepsy; steals; incorrigible	10/30/31	101	101	..	..	0	0	Conduct better in home and school; no spells
W. R.	15	M	1924	Concussion	+	+	Housebreaker; runaway	3/19/31	123	135	25	10	0	0	Behavior good
E. B.	47	M	1931	Concussion	+	+	Unable to work; ringing in ears	10/27/32	140	140	40	12	0	0	9/22/33 entirely well; working
P. F.	12	M	1930	Concussion	+	0	Convulsions	4/ 1/31	110	115	28	4	0	0	No convulsions until 2/24/32; then epileptic psychic equivalent developed; now in Selingsgrove
H. S.	17	F	1925	Concussion	+	+	Thief; runaway	8/24/33	122	122	30	16	0	0	Behavior improved; doing well at Sleighton Farms
W. M.	23	M	1930	Concussion	+	+	Criminal; housebreaker	7/29/30	104	144	18	12	+	+	Unimproved
S. N.	52	M	1930	Concussion	+	+	Irritable	12/16/32	145	145	36	12	0	0	Still irritable
J. P.	14	M	1920	Concussion	0	0	Convulsions; incorrigible; truant	6/15/33	146	146	18	6	0	0	No convulsions since treatment; behavior good
P. B.	10	M	1928	Concussion	0	+	Convulsions	7/24/31	80	92	20	7	..	0	No convulsions since treatment
C. O.	15	M	1930	Concussion; acute encephalitis in 1931	+	+	Convulsions	2/28/33	108	108	30	20	0	0	No convulsions
W. P.	14	M	1932	Fracture and concussion	+	+	Irritable	4/27/32	110	120	32	10	+	+	No improvement
W. S.	45	M	1931	Fracture	+	+	Paranoid psychosis	6/28/32	165	150	34	22	0	0	Still mildly paranoid
J. M.	13	M	1923	Fracture	+	+	Steals; irritable	8/20/29	70	70	20	10	0	0	Behavior good since treatment
W. K.	21	M	1931	Concussion	+	+	Epileptic psychic equivalents	2/11/33	122	142	32	8	0	0	Still has epileptic psychic equivalents; in Byberry
I. S.	12	M	1927	Concussion	+	+	Irritable; behavior problem in school	1/21/30	75	85	10	12	0	0	Doing well in school
J. W.	15	F	1926	Concussion	+	+	Irritable; sex offenses	1/ 9/31	120	115	28	12	0	0	Improved for about one year; cerebrospinal fluid pressure high; relapse
R. O.	8	M	1930	Laceration of head after severe blow; vomiting	+	+	Irritable; retarded in school after injury	8/23/32	78	82	38	10	0	0	
J. M.	21	M	1931	Concussion	+	+	Irritable; fights	1/20/32	160	150	23	20	0	0	Improved
H. T.	12	M	1927	Concussion	+	+	Restless; hyperactive; incorrigible	6/10/30	100	100	24	18	0	0	Behavior good since treatment

CONCLUSIONS

The therapeutic results obtained from pneumocranium in the treatment for posttraumatic headache, dizziness and change in character prove that this syndrome is organic rather than functional. The diagnosis of traumatic neurosis is usually unjustifiable if the patient gives a history of cerebral concussion. On the whole, lumbar insufflation of air is a safe and satisfactory method of treatment for posttraumatic sequelae.

DISCUSSION

DR. DAVIDSON: During the past three years practically all the juvenile delinquents of Philadelphia have passed through my hands. One cause of delinquency in children stands out concretely, namely, cerebral trauma causing change in character. Many of the children who steal owing to change in character come from a social class in which there is no necessity for stealing and in which environmental companionship is not a bad influence. These boys frequently associate with boys of a decidedly lower social scale. Their offenses are peculiar in that they are never committed for gain. It seems that these children steal for excitement and that they are impelled by some obscure mental force. Almost invariably they give away the proceeds of their robberies, and they seldom show any desire for profit. The history in these cases is rather characteristic. The boys are normal until a few weeks or months or even a year following a severe head injury. The parents begin to notice a change in behavior in the home. The patient fights unnecessarily with siblings, becomes destructive in a wanton fashion, may use foul language and begins to keep late hours. He frequently absents himself from home for days at a time. Reports of bad school work come in. The teacher complains that the child is noisy, unruly, vulgar or perhaps obscene and that he fails to learn. Subjectively the patient complains of headache, dizziness and occasionally of "a queer feeling in the head." The dizziness and headache are particularly prone to appear following the ordinary exertions of childhood, e. g., running.

Pneumocranium has been exceedingly beneficial in removing the symptoms, both subjectively and objectively. Seldom do children thus treated come back into court. They lose the headaches and dizziness, sometimes temporarily but sometimes apparently permanently. A striking feature is that following pneumocranium the first remark made by many of the patients is: "I have lost that bad feeling." This answer has been made to the simple question: "How do you feel?" without any lead whatever.

I have seen some results of pneumocranium in adults. The patients have been benefited considerably, some only temporarily but some apparently permanently. Whether the relief is temporary or permanent practically all the patients lose their restlessness and aversion to noise. It appears to me that the report presented is reasonable in assuming that pneumocranium has an important therapeutic value in cases of cerebral trauma in which headache and dizziness, but especially changes in character, are sequelae.

DR. L. H. SMITH: The significance of the history of concussion often given should not be overlooked as a possible causative factor of the change in personality or character. I believe that in many other types of medical cases, if the history is properly secured, it will be found that a certain number of accidents and possible concussions are reported which have no relation to the illnesses complained of. The history given by parents of children with postencephalitic disorders is often carried back to some injury to the head. Probably such an injury is too often brought in as the etiology. To my mind any case of concussion with a period,

short or long, of unconsciousness is a definitely organic condition. I see no basis on which one can secure results in such a case unless one prescribes treatment on an organic basis.

Another indeterminate feature in the treatment of such patients concerns the effect of general supervision and management of the general living program. One may benefit them far more than one realizes by simply helping them to readjust better to a more hygienic type of living.

I do not understand what physiologic effects the introduction of air into the spinal fluid cavities can have. Whether the introduction of the air or other phases of the treatment are considered, there is some physical or psychologic effect, but it is more important to know whether or not the result is from an organic or a functional change. I always feel insecure in treating such patients when a result is obtained, as I do not know from what source the particular result originated.

DR. LONG: To what does Dr. Drayton attribute the improvement in these cases?

DR. KEYES: Has this treatment been used in the postencephalitic behavior cases? What was the age of the youngest patient treated?

DR. DRAYTON: I have treated two or three children with sequelae of both concussion and encephalitis. The headache and dizziness were relieved in these cases, but the change in character was unaltered. The possibility that constant medical observation may be of physiologic benefit in such cases need not be seriously considered. Although I have kept in touch with many of them for four or five years, the contact has not always been personal. In some cases I have received reports from insurance companies, in others from probation officers, while many patients report to the clinic every six months.

A boy from New Jersey had been in so much trouble following a cerebral concussion that he was sent to a home for the feebleminded. He said that he had no headache but that he was very dizzy. Three weeks after an encephalogram was made he came to me and said, "You asked me if I had a headache. I said that I didn't because I thought that every one's head felt that way." He was able to spin around on his toes without any ill effects. Shortly afterward he secured a job. Later he obtained a motor boat and now makes his living by taking out fishing parties. I do not think that the result was psychologic.

Dr. Alpers asked about the effect of change of environment. The majority of the improved patients have not changed their environment but have returned home. However, some have been placed. Two or three have been sent to Glen Mills, and the discipline may have accounted for the improvement in behavior. Many of the children come from good homes. Often it is stated that the child was formerly well behaved in school but became uncontrollable after the head injury. Following the encephalogram the patient gave no more trouble in school.

In reply to Dr. Long I cannot explain how the improvement following encephalography is brought about.

Abstracts from Current Literature

A Malignant Neurinoma (Schwannoma) with Epithelial Elements. W. W. Brandes, Arch. Path. **16**:649 (Nov.) 1933.

Tumors arising from peripheral nerves in which epithelial elements were present have been reported by Cohn, Stewart and Copeland and Masson. The presence of such elements is in favor of the point of view that these tumors arise from the sheath of Schwann, which is of ectodermal origin, rather than from the endoneurium or the perineurium, which are mesodermal structures. Nageotte and Masson pointed out the similarities between spontaneously occurring tumors of nerves, experimentally produced schwannomas and regenerating nerves. Verocay described circumscribed proliferations of Schwann's cells which he believed were the forerunners of these tumors. He stressed the variations in the staining of the fibrils with Van Gieson's stain; Masson also demonstrated that many of them stain differently from true collagenous fibers with trichrome stains. There is considerable evidence that many of these tumors arise from the neurilemma and that the collagenous-like fibers in these tumors and the endoneurium in normal nerves in part may be formed by the Schwann cells. One can explain the presence of epithelium-like structures in some of these tumors much more readily on the supposition that they arise from the neurilemma than on the theory that they originate from mesodermal elements.

The case reported is of interest from several points of view. Clinically, the tumor was of rapid growth, in a man aged 73, with pain present for five months as the chief symptom. Histologically the tumor presented features of a neurogenic sarcoma, throughout which there were scattered small masses of epithelial-like cells. Metastases involved the regional lymph nodes and the lungs particularly, and were composed of cells like those in the epithelial masses in the primary tumor. Myxomatous degeneration was a marked feature, especially in the central portion of the primary tumor and less so in the metastases.

Histologic examination of the tumor in the thigh gave rather confusing results, but definitely ruled out certain possibilities. The greater portion was composed of a sarcomatous-appearing stroma presenting the features seen in neurogenic sarcomas. Intertwining bundles of elongated fibrils with varying numbers of nuclei, some of which were very much elongated, were seen in the compact areas. Some of these bundles of fibers were much swollen and had compressed the surrounding tissue slightly. This swelling seems to have been due to myxomatous degeneration, which was marked, especially in the more central portions of the tumor. The length and the thickness of the fibrils varied markedly. Many small fine fibrils could be seen between fibrils having a parallel course. With Van Gieson's stain there was considerable variation in the tinctorial reaction, which ranged from yellow to orange to deep red. In the photomicrograph shown, cells in varying stages of degeneration could be seen between parallel fibers. The fibers were applied to the surface of the cell so that it appeared as though they were laid down along the surface of the cell columns in an arrangement similar to that described by Masson for experimental schwannomas. In some regions a suggestion of a palisade-like arrangement of nuclei could be seen.

Some long fibrils were not directly associated with nuclei, whereas others had several associated with them in linear fashion. Many of the nuclei were elongated, at times bent on themselves and frequently fissured and irregular in contour. Nucleoli were prominent in a large number of these cells. The number of nuclei varied considerably in different regions. In more cellular areas many nuclei were hyperchromatic, and mitotic figures were present in moderate numbers. The cells varied much in size and shape. Not infrequently nucleated cytoplasmic masses were connected by cytoplasmic processes, which suggested a syncytial character of some portions of the tumor.

A most interesting histologic feature of the tumor was the presence of fairly uniformly distributed round, oval and elongated epithelium-like masses. Some of these were solid masses composed of cells that simulated pavement cells; others had cuboidal and flattened cells arranged about a lumen. In some instances long, narrow, solid cords of epithelial cells were seen which must have been longitudinal segments of the tubular structures. The nuclei in some of these solid masses were perpendicularly arranged and were interesting in comparison with a similar feature in the embryonic Schwann membrane.

The metastases in the lymph glands were composed entirely of cells similar to the epithelial-like cells in the tumor in the thigh. The cells were large; their borders were frequently indistinct, and in many of them the cytoplasm was vacuolated. The nuclei were large, irregular and frequently lobulated or fissured, with prominent nucleoli. Small areas with a myxomatous appearance similar to the stroma of the main tumor were seen in several of the nodules in the lung, demonstrating that the epithelium-like metastases had undergone changes similar to those in the primary tumor. The metastases in the lungs also contained only the epithelial-like cells. Extensive central necrosis had occurred in the largest nodes.

WINKELMAN, Philadelphia.

A CENTRAL VISION SCOTOMETER. C. E. FERREE and G. RAND, Arch. Ophth. **9**:608 (April) 1933.

The mapping, and even the detection, of small central scotomas is one of the outstanding problems in perimetry. In cases of low acuity it is important to determine whether a central scotoma is present. The authors state that with their new device they have been able to detect scotomas which they failed to find with the tangent screen. Further, that in no case did they fail to discover a scotoma that had been disclosed by other apparatuses.

The features and advantages of the instrument may be summarized as follows: 1. The determination can be made in but a small fraction of the time required for an examination with the tangent screen. With the eye in position, no more time is required than to look at the stimulus presented. The ease and quickness with which the examination can be made are of particularly great advantage in cases in which the patient is too ill for an examination with the tangent screen. 2. Sensitive means are provided for the detection of scotomas of different degrees of density, and also for a determination of their approximate size. Colored stimuli, which are graded as to size, and form stimuli, which are graded as to both size and relation to background, are used. 3. The determinations are made with the correct control of preexposure and the surrounding field. For colored stimuli, the preexposure and surrounding field are of a gray, the brightness of the color in central vision for the intensity of illumination and the size of the pupil used, and for the form stimuli, the preexposure is of the brightness of the surrounding field. 4. Convenient mechanical means are provided for the control of both the preexposure and the length of exposure, and also for applying an objective check on the correctness of the judgment. 5. The test surfaces are uniformly illuminated with light corrected to daylight color. Means are provided for varying the intensity of illumination. However, the effective illumination can be held constant at 7 foot-candles, as is done in the Ferree-Rand perimeter, if that is desired. 6. The determination is rendered practically independent of the condition of refraction without the inconvenience and disturbance attending the wearing of correcting glasses. In an examination for central scotoma, the elimination of the influence of a refractive condition is of great importance. 7. Fixation is controlled by the vision of the eye under examination. Reliance does not have to be placed on the control afforded by coordination with the fixation of the eye not under examination. In this connection it may be noted that the eye not under examination also frequently has a central scotoma. 8. A stationary stimulus with a controlled exposure is used. The errors attending the use of a moving stimulus are thus avoided. It is extremely difficult to detect very small central scotomas

on the tangent screen, even with the best control of fixation and under the most favorable conditions of presentation of stimulus that can be obtained.

The apparatus consists of two disks, the purpose of the first to provide a conveniently operable device for the presentation of the color and form stimuli selected for the examination, the preexposure necessary and the blank surfaces for an objective check on the judgment. The second disk provides the background on which the stimulus is to be viewed and the control of the brightness of the more immediately surrounding field, and contains the apertures needed for the gradation of the size of the stimulus. In front of these two disks is a stationary plate, which provides control of the brightness of the more remote surrounding fields and contains the device for the control of fixation. The entire apparatus is mounted at one end of a horizontal bar. At the other is mounted the eyepiece, which is provided with a pupillary aperture of an optimum size for eliminating errors in refraction and for giving the highest possible acuity.

The instrument is inexpensive, requires a small amount of space and is exceedingly simple and easy to operate. The rather important factor of preexposure is satisfactorily arranged, in that preexposure may be repeatedly alternated with the stimulus sector. If the patient fails to discriminate the stimulus used, the examination is repeated with the larger size. If the stimulus is seen with either of these larger sizes, one of two conclusions may be drawn: Either the scotoma is smaller than the stimulus seen or the stimulus is of a degree of visibility which is supraliminal for the defective area. In the former case, only a rim or bit of the stimulus will be seen as of normal or nearly normal visibility; in the latter, the stimulus will appear of reduced visibility.

SPAETH, Philadelphia.

PSEUDOTABES (THE CONSTELLATIVE INFLUENCE OF SYPHILIS, LEAD AND MORPHINE). IDA SILBERPFENNIG, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **35**:169, 1933.

A man, aged 57, a painter's helper, contracted syphilis in 1894, for which he was given several courses of mercury and arsphenamine sixteen and twenty years, respectively, after the infection. In 1907, he had severe attacks of lead colic, for which he received large doses of morphine. The attacks ceased in 1908. He remained well until after the World War, when he began to have boring pains in both lower extremities, followed by pains in the lower portion of the abdomen. These persisted till 1932, when the pains became especially severe in the region of the bladder and he began to have difficulty in urination. In 1928 he had been suspected of having neurosyphilis and was accordingly subjected to malariotherapy.

On admission to the hospital in 1924, the patient stated that the maximum dose of morphine that he had received was 0.04 Gm. At that time examination disclosed: slight cyanosis, somewhat tortuous radial arteries, a rapid pulse, a mitral systolic murmur, an impure aortic second sound and blood pressure of 130; the abdomen was soft and not tender. The positive neurologic signs were: Argyll Robertson pupils, positive Abadie and Biernacki signs and unsteady gait; there was also a fine tremor of the outstretched fingers. Later, there appeared zones of hyperesthesia over the trunk between the third and the tenth thoracic segment, and in the lower extremities involving the upper lumbar radicular distribution; between these zones of hyperesthesia there were vague areas of hypesthesia and hypalgesia. There were no disturbances in posterior column sensibility. The Wassermann reaction was negative with both blood and spinal fluid; the Pandy test was positive; the Nonne-Appelt test, negative; the cerebrospinal fluid contained 2 lymphocytes per cubic millimeter; the colloidal gold curve was in the syphilitic zone. On one occasion the urine showed traces of lead; the red blood cells showed no stippling. Roentgenographic examination of the gastro-intestinal tract showed a spastic contracture of the descending colon.

The patient complained of severe pains and asked repeatedly for injections of morphine. In September 1932, the general condition became worse; cystitis developed, and the patient died of exhaustion and pneumonia. The clinical diagnosis was: tabes dorsalis and syphilitic mesaortitis.

Histologic examination of the lowermost segments of the cord revealed an extraspinal degeneration of the posterior nerve roots, especially in the median portion, which was much more marked than the degeneration of the posterior columns. The degeneration was most intense in the sacral portion of the cord and diminished gradually as it ascended cephalad. The histologic picture was different in the dorsal portion of the cord; here, though the middle root zone was still affected, the change was patchy and independent of the degeneration in the lateral portions of the column of Burdach. In the lowermost segments of the cervical region of the cord, the column of Goll showed practically no degeneration, whereas degeneration in the regions adjacent to the root entrance zones was strikingly well marked. In the region of the fourth cervical segment there was an independent focus of degeneration involving chiefly the lateral portion of the column of Goll and the mesial portion of the column of Burdach. The larger spinal vessels showed thickening of the middle coat, with homogenization, slight intimal proliferation and in places perivascular infiltration as well as a striking thickening of the capillaries. The vascular changes were most marked within the areas of degeneration and within the septum. The vessels within the roots were somewhat sclerotic, and the smallest vessels were surrounded by glial nodules indicative of a more or less older pathologic process.

The pallidum showed symmetrical softenings, 4 mm. wide and 6 mm. long; these were most numerous in the mesial portion of this ganglion adjacent to the internal capsule; these foci resembled those observed in the pallidum and substantia nigra in cases of gas poisoning.

The histologic changes, taken in conjunction with the clinical history, are attributed to the combined effects of lead, syphilis and morphine. The tabiform disease in the cord is attributed either to a primary degeneration of the root or to vascular disease, more likely to the latter. The absence of clinical symptoms referable to the marked involvement of the pallidum is commented on.

KESCHNER, New York.

NOBEL PRIZE IN MEDICINE FOR 1932 AWARDED TO SHERRINGTON AND ADRIAN. EDITORIAL, J. A. M. A. **99**:1693 (Nov. 12) 1932.

The Nobel Prize in Medicine for 1932 has been awarded to two British investigators, Sir Charles Scott Sherrington, professor of physiology at Oxford University, and Dr. Edgar Douglas Adrian, professor of physiology at Cambridge University. The honor bestowed on Professor Sherrington is a belated recognition, by the Nobel Prize Committee, of his many monumental contributions to knowledge of the physiology of the nervous system made during the past forty years. Early in his career he mapped out the motor area of the cerebral cortex of the chimpanzee, thus establishing the character of cerebral localization of function. Another important discovery made by him was that of decerebrate rigidity—an extensor hypertonus of the legs of a mammal following the section of the brain stem just above the pons. This discovery led to the epoch-making work of Magnus and his associates in body righting and postural reflexes. Professor Sherrington is perhaps best known for his thoroughgoing study of the reflex equipment of the "spinal" mammal, in which he discovered the phenomenon of "reciprocal innervation," a reflex relaxation of one muscle or set of muscles simultaneously with the contraction of another group of muscles, the two groups constituting anatomic antagonists. Thus, flexors and extensors, instead of working against each other, actually are made to work together in the execution of both flexion and extension, which results in the movements being carried out with a greater degree of exactitude than would be possible by the action of one group alone. His work on the spinal mammal was reported in a series of lectures given at Yale University and published in 1906 under the title "Integrative Action of the Nervous System," which has become one of the classics of physiologic research. That other scientific bodies were not so tardy in recognizing Professor Sherrington's accomplishments is shown by his election to the presidency of the Royal

Society, his membership in many foreign scientific societies, including the National Academy of Science at Washington, and the bestowal on him of honorary degrees by seventeen universities.

Adrian's researches began on the isolated peripheral nerve. At first, with Lucas, he clarified much of the behavior of nerves in transmitting crucial messages. The index of a propagated nerve impulse was here the contraction of an attached muscle and failed to discriminate the action of an individual axon from the total. With the advent of a practical amplifying technic, however, the nerve action currents could be studied with a precision not before possible, and Adrian utilized these in his further analysis. Single nerve fibers were activated by normal stimulation of single end organs, or after destruction of the connections of all but one. Detailed information on mechanisms of sensory stimulation rapidly resulted, and the general relationship, that stimulus intensity is reflected in afferent impulse frequency, clearly emerged.

One of the first fruits of Sherrington's later approach was the delineation (in cats) of the myotatic, or stretch, reflex, not unrelated to his earlier discovery of decerebrate rigidity. Pull on the tendon of a muscle led to reflex shortening in response to continued tension, as in posture and tone of antigravity muscles. Adrian obtained his first success with single end organs by pulling a frog's muscle and recording the volley set up in a single afferent fiber. These studies resulted in a clearer picture of reflex tone that helped to settle the cloudiness of conceptions of this problem. Many clinical neurologists as well as physiologists have been interested in this work, for spasticities contribute greatly to human invalidism. Neurologists have followed his work with their own researches on the disturbances in tone mechanism appearing in disease.

The discharge of motor neurons also was investigated by the electrical and mechanical technics, and complementary information was obtained. The occurrence of distinct, spontaneous and rhythmic changes in electrical state and irritability of ganglion cells was an important observation. It cannot fail to be of profound significance that receptor organs and nerve cells and, barring striking quantitative differences, the nerve fiber itself have been shown to function on the same simple plan. Professors Sherrington and Adrian have made significant additions to knowledge of the dynamics of the normal nervous system, a knowledge that is basic for diagnosis and therapy in nervous disorders. EDITOR'S ABSTRACT.

INTRACRANIAL HYPERTENSION NOT CAUSED BY CEREBRAL TUMORS AND THE ACOUSTIC NERVE. N. METZIANU, N. JONESCO-SISESTI, TZETZU and D. BORS, Rev. d'oto-neuro-opht. **11**:721 (Dec.) 1933.

In the internal auditory meatus the auditory and facial nerves and the intermediary nerve of Wrisberg are enveloped in the same layer of arachnoid membrane. They next traverse the space between the cranium and the cerebral trunk, where they are bathed directly in the cerebrospinal fluid. In the brain stem, Deiters', Roller's and the triangular nuclei are almost subjacent to the ependyma of the fourth ventricle, and the stria acusticus lies on its floor; the cochlear pathways terminate in a cortical center. At all of these places the nerve tracts are directly exposed to the influence of hypertension of the cerebrospinal fluid.

The causes, other than neoplasms, of intracranial hypertension are: (1) acute or chronic meningitis, (2) cerebral arachnoiditis, (3) cerebral parasitosis (cysticercus), (4) trauma (hemorrhage), (5) congenital malformations (imperforate aqueduct of Sylvius), (6) disturbances of the venous circulation, both inside and outside the cranium (thrombosis of the intracranial veins, asystole) and (7) diverse causes, such as uremia, lead poisoning, arterial hypertension and intestinal parasitosis.

After the optic nerve, the auditory nerve is most sensitive to hypertension, and the vestibular portion is more vulnerable than the cochlear. There is no parallelism between the intensity of the cochleovestibular syndrome and the degree of hypertension. Factors other than pure hypertension determine the production of the

acoustic phenomena: a particular fragility of the cochleovestibular apparatus, a congenital predisposition or a peculiar neurovegetative constitution.

Vestibular disturbances are more frequent in cases of hypertension caused by chronic meningitis than in those resulting from the acute form. Spontaneous nystagmus and vertigo are the prominent signs; they are accompanied by hypo-excitability to caloric stimulation with almost normal reactions to rotation and to galvanism. In hypertension from arachnoiditis, the rapidity of the development of the hypertensive syndrome depends on the location of the arachnoiditis. Cochleo-vestibular signs in this condition are hyperacusis or hypo-acusis and global or partial vestibular hypo-excitability. Monier-Vinard, Ramadier and Chaussé have reported a case of cystic arachnoiditis of one pontocerebellar angle that was accompanied by bilateral cochleovestibular disturbances. According to Aubry, the effect of hypertension on the eighth nerve varies with the stage of evolution of the process. In the first stage there is pure stasis, characterized by slight functional labyrinthine disturbances. In the second stage lesions analogous to those observed in optic neuritis occur and are characterized by increase of vestibular disturbances, absence of vertigo reaction and hyporeflectivity in the caloric test; later they are characterized by much diminished reactions in the rotation test. Finally, there is diminution of reaction in the galvanic test.

Hypertension from parasitic cysts depends on the size of the cysts, their multiplicity or their location. Smite considers that vestibular disturbances in cases of cerebral cysticercosis are due to hydrocephalus. They are characterized by abnormal attitudes of the head and by exaggeration of the headache, vertigo and vomiting with certain movements or changes of position of the head. These signs are found also in certain cases of tumor of the fourth ventricle. In all cases of intracranial hemorrhage, hypertension occurs. Its signs are usually masked by other grave symptoms. The sequelae of cranial traumatism include vestibular disturbances, which occur in repeated attacks, caused by transient hypertension. Lumbar puncture gives temporary relief. It is probable that in cases of arterio-sclerosis, uremia and lead poisoning, vestibular symptoms, when present, are caused by slight persistent or transitory hypertension of the cerebrospinal fluid.

Three conditions explain the cochleovestibular disturbances created by intra-cranial hypertension: direct compression of the nerve trunk, compression of the endolymphatic sac and compression of the vestibular and cochlear central neurons. In many cases hypertension of the endolymph and of the cerebrospinal fluid coexist. Intracranial hypertension alone is not always responsible for cochleovestibular phenomena. Other factors are irritation from toxic foci, regional arachnoiditis, compression from cysts, local traumatic lesions and vascular fragility in such diseases as diabetes, uremia, arteriosclerosis and saturnism.

DENNIS, Colorado Springs, Colo.

EVERYDAY PSYCHOLOGY OF THE NORMAL CHILD. EDWARD A. STRECKER, Ment. Hyg. **17**:65 (Jan.) 1933.

The child must draw on the environment for the satisfaction of its psychologic needs; a deprivation or inadequacy of this psychic foodstuff will injure the child's personality. To develop a wholesome personality certain needs must be met—stimuli drawn for the most part from the postnatal environment. First of these is the need for physical motion; a child prevented from exploring the environment by movement will suffer a deficiency in the stream of incoming stimuli—and consequently will be mentally or emotionally retarded. A quiet boy or girl is a good, but not a sound, child. Second to motion is the group of influences embracing imitation, identification, idealization and suggestibility. The acquisition of ability to talk is, in normal children, largely a process of imitation. Since children are unable to make fine ethical distinctions, they add to their personality structures many layers of both good and bad qualities by this process. Probably the emotional force behind imitation is largely one of identification with the idealized parent or guardian. This tendency presents one of the most delicate problems in child

guidance: the maintenance of the parent ideal. If the ideal crashes too soon, the child loses confidence and stability in his world; if it persists too long, the child becomes tragically dependent on the parent, teacher, or parent-surrogate. Less direct than imitation is the inclination toward certain behavior patterns produced by suggestibility.

The conditioning of reflexes deserves some consideration in child guidance. Much nervousness, indigestion, insomnia and enuresis represents bad conditioning. For example, bedtime may be associated with hilarity or excitement instead of peace and calm. Unsuccessful punishment is often the result of improper conditioning. Cruel, retaliative, delayed or promised-but-unfulfilled punishment is futile because it fails to associate, in time or proportion, the offense and the result. Distortions in the normal will-to-power are also responsible for many childhood behavior problems. For example, the transition from pampered convalescence to normal health may be difficult because of the swing to one extreme—deflation—or the other—overemphasis. In the first instance the child, brought harshly to realize that his days of power are over, is frightened and made permanently cynical or hard; in the latter instance the child is spoiled and made unreliant and dependent.

Curiosity is a normal and desirable childhood trait. It should be met by simple and truthful answers. Questions about sexual functions should be answered with the same casualness as meets all other questions. Another juvenile trait needing attention is the tendency toward savagery. This is a condensed replica of the human savage state through which we have passed on the road to civilization. It is by proper exploitation of this quality that we may develop love of nature, courage, physical strength, fair competition and self-reliance. Since every adolescent sooner or later must enter into a competitive world, the desire to win, and to win fairly, should be inculcated early in life. Finally, that budding of the faculty of imagination—romancing—should be mixed with truthfulness yet received with respect.

These potentials must be fitted together skilfully to produce the wholesome personality. They form the stream of environment. And the environment of the child is in the hands of the adult.

DAVIDSON, Newark, N. J.

PAINFUL SYNDROME OF TUMORS OF THE APEX OF THE ORBIT (PERSISTENT HEADACHE AND PAINFUL ANESTHESIA). J. SEDAN, Ann. d'ocul. **170**:846 (Oct.) 1933.

The syndrome of the sphenoid fissure is a definite clinical picture, which was first described in detail by Rochon-Duvigneaud in 1896. As the optic canal participates, Rollet preferred the term "syndrome of the orbital apex." Roger, of Marseilles, appears to have been the first to emphasize the association of headache with this syndrome. Having examined eight patients with manifestations of this type, Roger found that headache was constant and was the most conspicuous symptom in the clinical picture. Being little troubled by reduction in visual acuity or by diplopia, because of ptosis, patients usually complained only of severe headache, which was the first symptom noticed.

In the *Revue d'oto-neuro-oculistique* a complete study was reported of headaches in the syndrome of the sphenoid fissure, with a description of the location of the pain (generally temporoparietal), of the evolution (usually progressive and almost always preceding ocular disturbances), of the intensity (ordinarily violent, with active paroxysms) and of the duration of some particular aspects, such as the aggravating influence of lateral decubitus. The sensibility of the cornea is rarely destroyed, but hypesthesia is commonly observed. Neuroparalytic keratitis is rare.

Sedan cites some previously unpublished facts on painful anesthesia and reports four cases of pituitary tumor involving the orbit through the sphenoid fissure (two sarcomas and two epitheliomas). All of the four patients complained of severe headaches in the beginning of the disease and later of facial pain. The fourth patient had pain, at first exclusively in the temporofrontoparietal region, associated

with almost complete cutaneous anesthesia in this area. He began to complain of pain in the lacrimal region, particularly at the time when this region began to lose its sensibility. The pains seemed to increase in proportion to the anesthesia. It is remarkable that the painful anesthesia subsided four times after operation in the four cases, which made it possible to find and remove the tumors, at least the orbital part, with section of all the sensory fibers. In spite of the interventions, followed twice by radium and twice by roentgen therapy, two of the patients died, but they died without headache or cutaneous pain. Immediately after the operation the anesthetic areas were no longer painful.

Everything seems to indicate that the tumor in compressing the nerve produces an incomplete physiologic section, and the last reaction in the nerve is spontaneous pain, even when all reaction to pain and provoked sensibility has disappeared.

This special aspect of pain in tumors of the orbital apex is presented because it has not been emphasized previously and because it may be of interest to read in a journal of ophthalmology the neurologic work of Roger emphasizing the importance of headache in the early diagnosis of orbital tumors.

BERENS, New York.

TREATMENT OF RESPIRATORY FAILURE IN ACUTE EPIDEMIC POLIOMYELITIS. M. BERNARD BRAHDY and M. LENARSKY, Am. J. Dis. Child. **46**:705 (Oct.) 1933.

A report is made on forty-six patients with respiratory embarrassment due to poliomyelitis, who were treated in a Drinker respirator. A few of the patients had bulbar lesions, but after a short trial they were not considered suitable for treatment by this method. The patients treated varied in age from 14 months to 24 years. The youngest patient to survive was 3 years of age. There were eighteen females and twenty-six males. The patients were divided into two groups: Those with involvement of the diaphragm and intercostal muscles were classified as having spinal lesions and those with involvement of the cranial nerves in whom the respiratory center was presumably affected were classified as having bulbar lesions. All of the patients with bulbar lesions died. Sixteen of the thirty-four patients with spinal lesions died in the respirator. The average duration of difficulty in breathing among the patients who survived was forty-six hours. The patients with spinal lesions who died had had respiratory difficulty for an average of sixteen hours before they were placed in the respirator. Ten of the patients with bulbar lesions averaged only three hours' duration of respiratory weakness. The authors think that the patient who survives the first two days in the respirator has a good chance to recover respiratory function. It was considered that in the cases of patients with continued high fever the prognosis was bad. Most of the patients who survived had a temperature of less than 101 F. after the third day. All showed some increase in the pulse rate. The cell counts of the spinal fluids in the various groups were not significantly different, although they varied from less than 60 to over 1,140. In patients with respiratory difficulty there is usually a loss of the normal elasticity of the lungs, with a suggestion of emphysema and thinning and often rupture of the alveolar walls. The authors emphasize that good nursing care has almost equal value with the use of the respirator. They also point out the necessity of preventing a rise in temperature of the air inside the respirator and the possible necessity of postural drainage. Removal of the patient from the respirator was done slowly, in many cases letting the patient breathe for himself while the motor of the respirator was still running. The authors do not advise the treatment of patients with slight or moderate respiratory distress in the respirator, but advise repeated small doses of sedatives and continued reassurance. They do not advise treatment in the respirator for a long period after sufficient respiratory function has returned to permit the patient to lie comfortably in bed. They think that the Drinker respirator represents an outstanding advance in treatment for respiratory failure in poliomyelitis.

WAGGONER, Ann Arbor, Mich.

SIGNIFICANCE AND TREATMENT OF SCIATIC PAIN. W. McK. CRAIG and R. K. GHORMLEY, J. A. M. A. **100**:1143 (April 15) 1933.

Craig and Ghormley state that sciatica, or sciatic pain, may be a symptom of constitutional or systemic disease, of tumor or inflammation of the spinal cord or nerve, of derangement or inflammatory reaction about the lumbar vertebrae, intervertebral foramina or sacro-iliac joint, or the result of postural strain. In the treatment of so painful a lesion, the contributory etiologic factors must be considered and eliminated if possible. There is a large group of cases in which the sciatic pain is of uncertain pathogenesis, and efforts have been made to distinguish between sciatic neuritis and sciatic neuralgia. This may be possible clinically, but the authors are unable to find specific treatment separately applicable to the two conditions. For the purpose of expediency, they divided the methods of treatment of sciatica into ambulatory and institutional. Many patients are unable, for economic and other reasons, to go to a hospital, and although the institutional form of treatment is the more efficacious, a certain proportion of the patients can be treated successfully by ambulant methods. Institutional treatment can be used alone or for the purpose of supplementing ambulant treatment. Their results of the ambulant forms of treatment are as follows: Epidural injection was done in eighty cases; in 52 per cent relief was complete; in 24 per cent it was moderate, and in 22 per cent there was no relief. Diathermy was instituted in thirty-six cases; 33 per cent of the patients were completely relieved; 12 per cent were moderately relieved, and in 55 per cent there was no relief. Epidural injection and diathermy were applied in twenty-one cases; in 42 per cent there was complete relief; there was moderate relief in 10 per cent and no relief in 48 per cent. A sacro-iliac belt and diathermy were employed in fifty-two cases; relief was complete in 32.6 per cent, moderate in 13 per cent, and in 54.4 per cent there was no relief. Epidural injection, a belt and diathermy were employed in eight cases; 85 per cent of the patient were completely relieved; 2 per cent were moderately relieved, and 13 per cent were not relieved. Results of treatment of patients confined to bed were as follows: In twenty-eight cases the following measures were employed: double Buck's extension, diathermy, epidural injections, intravenous injections of foreign protein and elimination of foci of infection. Of the twenty-two patients, 85.7 per cent were completely relieved and 14.3 per cent moderately relieved. The same measures were employed in fourteen, except that epidural injection was omitted; complete relief resulted in 63 per cent, moderate relief in 23 per cent and no relief in 14 per cent. EDITOR'S ABSTRACT.

THE INTERACTION OF HEREDITY AND ENVIRONMENT. LANCELOT HOGBEN, J. Ment. Sc. **79**:590, 1933.

The contributions of genetics to the study of social phenomena, including mental disease, are discussed in this article with intelligence, understanding and thoroughness. Advances in science are determined not only by the ability to ask questions but by the development of technics for answering them. The fact that the condition is congenital does not mean that the environment is of no etiologic significance. The intra-uterine environment has not usually been taken into consideration. The importance of intra-uterine environment is indicated by the high incidence of malformation in children born of mothers approaching the menopause and the frequency of certain conditions in first-born children. When the modus operandi of the genes is understood one will know the kind of knowledge needed to control the influence of the genes. Selection is not the only way in which heredity can be controlled. Hemophilia is a hereditary disease, but with ovarian hormone therapy it can be controlled in spite of the innate tendency for it to occur. The knowledge of the way in which one dominant gene produces its manifestations teaches how to prevent or further these manifestations. The same gene may be responsible for several varied traits. A great deal depends on the way in which the genes are combined. Thus, when two kinds of tropical fish are combined for the purpose of producing a new, more decorative breed, the effect is easily achieved, but there

also develops a certain tumor which was apparently carried as a recessive in the same gene which controlled pigmentation. When the method of genetics is transferred intelligently to psychiatry, interesting results are observed. Thus, Penrose (*J. Genetics* **25**:407 [April] 1932) found that the frequency with which mongolian idiots are born of mothers over 40 years of age compares to the theoretical 1:3 ratio, if one takes into consideration that mongolian idiots are likely to die before birth. Mental defect is not a unitary character. It is essentially a tail-end of a normal distribution of intelligence. It is a sociologic rather than a clinical concept. The freudian school performed a service to human biology by focusing attention on the importance of the social environment. In mental disease different mutations and different environments in different situations may be chiefly responsible for the same clinical entities. Mental disease, thus, is not a genetic problem alone; neither is it a single genetic problem. The division of disease into two groups, mental diseases which are due to heredity and bodily diseases which are due to environment, is a legacy of that period in the history of science when the study of the central nervous system belonged to the province of moral philosophy.

KASANIN, Howard, R. I.

CALIBER OF THE PUPIL IN HOMONYMOUS HEMIANOPIA. G. WEILL and J. NORDMANN, Rev. d'oto-neuro-opht. **11**:20 (Jan.) 1933.

Hemianopia always points to an interference in the optic pathways. While it is true that in a patient with bitemporal hemianopia a lesion of the chiasm may be inferred with much precision, localization in cases of homonymous hemianopia is not so precise. In the latter the lesion lies in the optic pathways above the chiasm, in either the optic tract, radiations, or the cortical center. The differential signs which have been abandoned or are not sufficiently substantiated (optokinetic nystagmus, which is said to be lacking in hemianopia of subcortical origin, for example) are not discussed. Primary optic atrophy and the hemianopic reflex of Wernicke are two valuable and reliable localizing signs. The former is characteristic of a lesion of the optic tract but cannot be recognized early with the ophthalmoscope. The latter, when positive, indicates a lesion of the optic tract. Thanks to the technic of Behr or Coppez, this reflex is more easily found to be clear and distinct.

A third sign has been described by Behr and confirmed by Schlesinger, Best and Bunge. This sign is that in hemianopia from a lesion of the optic tract, the pupil on the side opposite the side of the lesion will be larger and will react less well. Thus, when the larger pupil is on the same side as the hemianopia, the lesion is in the optic tract; when it is on the side opposite the hemianopia, the lesion will be cortical or subcortical. The authors studied this sign in eleven cases of homonymous hemianopia. In two the pupils were equal. Of the remaining nine cases, the hemianopia was cortical or subcortical in eight; this localization was confirmed in two by autopsy, in one by the location of a fracture of the skull with cerebral hernia, in four by the concomitant signs of alexia, agraphia or aphasia, and in one by the history of a previous uremic blindness. Of the three verified cases, the larger pupil was on the same side as the hemianopia in two; of the five probable cases, three did not support the claims of Behr. From these observations, Weill and Nordmann deny an absolute localizing value of the sign of anisocoria and ask whether the sign may not be analogous to that in cerebrospinal meningitis, coma and cranial traumatisms.

DENNIS, Colorado Springs, Colo.

CEREBRAL ANEURYSMS. C. R. TUTHILL, Arch. Path. **16**:630 (Nov.) 1933.

Forbus recently showed that an absence of media is found at the bifurcation of the cerebral and other arteries. In relation to this study he reported a case in which there were four small aneurysms at the branching of the cerebral vessels. He found no other vascular lesions and concluded that the aneurysms were con-

genital. He believed that such miliary or congenital aneurysms develop at the bifurcation of cerebral arteries in a medial defect. In the present paper are described six cases of aneurysms of the cerebral arteries in relation to lesions of the vessels of the circle of Willis and their branches.

Forbus distinguished a congenital aneurysm from an arteriosclerotic one by the absence of intimal changes in the wall of the vessel from which the aneurysm springs, and by the size and location of the aneurysm. Such an aneurysm is small and is situated in the fork bifurcating vessels.

There are presented five sacculated aneurysms of the large cerebral vessels, varying from the size of a small bean to that of a walnut. Three aneurysms were located at the branching of the vessels; one in the angle of bifurcation of the anterior cerebral artery, one in the anterior communicating artery and one in the angle of the bifurcation of the middle cerebral artery. Various stages of arteriosclerotic changes were observed in the walls of the aneurysms. In two cases there was an absence of arteriosclerotic growth in the intima of the vessels forming the aneurysm. However, these two aneurysms were considered arteriosclerotic because of the hyperplasia of the other cerebral vessels and because of localized absorption of fat in one or more of these areas. In a sixth case were found hyaline aneurysmal dilatations of the small arteries of the meninges and of the substance of the brain with rupture and small hemorrhages. No distinction could be made between arteriosclerotic and congenital aneurysms.

The so-called medial defects at the bifurcation of the vessels are explainable as embedding artefacts, because of the irregularity of the vascular bed and the twisting of the vessels from elasticity. It is suggested that the absorption of fat in the media underlying the absorption of fat in an area of split elastic and collagenous fibers at the branching of a vessel is the first stage in the formation of an aneurysm.

WINKELMAN, Philadelphia.

A CASE OF SYNDROME OF MONBRUN AND BENISTY (CAUSALGIA FROM THE OCULAR STUMP) CURED BY GASSERECTOMY. J.-A. BARRÉ and MARC KLEIN, Rev. d'oto-neuro-opht. **11**:755 (Dec.) 1933.

The essential characteristics of the syndrome of Monbrun and Benisty are pain, starting in the orbit a number of months after rupture of the eyeball from trauma and radiating to the corresponding half of the face or the skull. The pains are accompanied by a smarting sensation and redness and abundant sweating of the affected region. Removal of the stump of the eye does not affect the painful phenomena.

A case in point was that of a man whose eyeball ruptured in 1907. Three months afterward a dull pain occurred in the orbit; later it became more acute, spread to the vertex and temporal region and was accompanied by crises of exacerbation, flow of tears and redness of the orbital cavity. The suffering eventually became unendurable, and in 1928 alcoholization of the superior branch of the trigeminus nerve was done through the supra-orbital foramen. Relief was obtained for several months. In 1932, resection of the ocular stump, with removal of as much of the optic nerve as possible, gave no relief. It was decided to direct operative measures to the gasserian ganglion; this was done as thoroughly as possible and resulted in complete amelioration of all the painful and secretory phenomena. The success of this operation appeared to be more complete than an operation on the cervical sympathetic chain which had been done in a similar case. The suggestion is made that other causalgias may be benefited by operation on the corresponding spinal ganglia or posterior roots. Late complete resection of the stump is not curative, and it is not known why the causalgic syndrome appears only after certain cases of incomplete removal of the eyeball. The most peripheral part of the sympathetic nerve is perhaps endowed with great sensibility, and it may be that irritations (neuromas), which may develop there, are more apt to cause causalgic pains than those that involve the sympathetic fibers above the

ganglion. The question, then, of why these pains do not cease after section of the sympathetic nerve above the ciliary ganglion remains unanswered.

DENNIS, Colorado Springs, Colo.

PROGRESSIVE BULBAR PARALYSIS. MAX HELFAND, J. Nerv. & Ment. Dis. **78**:362 (Oct.) 1933.

Helfand has searched the literature from 1910 to the present for what was defined by Charcot, Duchenne and Oppenheim as progressive bulbar paralysis and has not found one genuine case of this syndrome uncomplicated by other symptoms and verified pathologically. Bulbar syndromes occur, of course as in poliomyelitis, arteriosclerosis, syphilis, tumors, vascular insults, multiple sclerosis and other conditions. Helfand reports the clinical and pathologic details in four cases which add doubt as to the existence of a disease entity called progressive bulbar paralysis, and he considers that the disease which has been described is merely a generalized morbid process of amyotrophic lateral sclerosis with a bulbar syndrome. In three of his four cases there were unmistakable findings of the latter disease, while only one case might be called true progressive bulbar paralysis, as it was unaccompanied by degeneration of the pyramidal tract. In the spinal cord the cells of the anterior horn are chiefly diseased while those in the lateral horn are more or less normal. The various nuclei of the medulla are involved in degenerative changes without any evidence of functional or phylogenetic predilection for amyotrophic lateral sclerosis; the cells of the spinal cord are chiefly involved, but an irregularity of localization should not serve as sufficient evidence to cause doubt as to the identity of one disease process in various cases. Almost every disseminated disease has localizable types without severing each from the main group. Cerebrospinal syphilis, multiple sclerosis and encephalitis pontis are cases in point. In amyotrophic lateral sclerosis the affinity of the toxin is less for mesodermal tissues than for the plasma of the nerve cell. Helfant concludes therefore that progressive bulbar paralysis is a syndrome of other disease entities, mostly of amyotrophic lateral sclerosis, in which the constellation of causative factors, including the process of senility, is most likely precipitated by an exogenic toxin which influences neural as well as mesodermal tissue.

HART, Greenwich, Conn.

AURAL VERTIGO: TREATMENT BY DIVISION OF EIGHTH NERVE. HUGH CAIRNS, Lancet **1**:946 (May 6) 1933.

The cases of four patients with severe aural vertigo treated by division of the auditory nerve are reported. With minor variations, the clinical picture was the same in all cases, and conformed to the classic description of Gowers. In each instance the patient had been growing deaf in one ear for some time before the attacks began. The attacks consisted of vertigo of sudden onset; three of the patients fell without warning, and the fourth frequently had a sensation of insecurity. In addition, external objects appeared to rotate; this symptom often was so aggravated by movement that the patients had to remain still, usually in a recumbent position. The vertigo persisted for several hours, was associated with vomiting in all but one case, and terminated in sleep. Each patient was incapacitated for at least one day during an attack. In the initial stage of the attacks one patient became completely blind for a moment, while another saw lights and stars; another felt intensely cold or hot, along with a feeling of impending doom. One patient, an instructor in drills, attributed his attacks to severe exertion, but the others could suggest no cause.

Milder reactions, unaccompanied by falling, occurred in all cases, and were often brought on by sudden movement of the head; in two patients mild attacks, described as "swimming of the head" and "giddiness on rising from the stooping position," occurred for some years before the severe attacks. All four patients have been relieved of their vertigo following the operation. They have returned to their original employment amidst noise and machinery.

Some of the physiologic results of the operation include vertigo and vomiting, which is quite transient. Nystagmus is present and is most striking to the opposite side. It persists in diminishing intensity for from two to three weeks. Diplopia, explained by the authors as due to skew deviation of the eyes, persisted intermittently for from one to three weeks.

BECK, Buffalo.

THE INFLUENCE OF INNERVATION ON THE GLYCOGEN METABOLISM OF THE MUSCLE. I. J. BAUM and E. PICHLER; II. J. BAUM, W. CHRISEN and E. PICHLER; III. O. LOEWI and E. PICHLER, Arch. f. d. ges. Physiol. **233**:35, 1933.

The denervated frog's muscle still forms glycogen; after extirpation of the pancreas about two thirds less, and after extirpation of the liver about one third less, is formed than in the denervated muscle of a normal animal. One-sided extirpation of the gastrocnemius muscle induces decrease of the glycogen content of the opposite gastrocnemius muscle (glycogenolytic reflex); sympathectomy on the side of the remaining gastrocnemius muscle prevents this decrease. Sympathectomy itself, however, induces an increase of the glycogen of the muscle. The authors suppose, therefore, that the glycogenolytic reflex is mediated not only through the sympathetic nerves, but also through the spinal nerves to the muscles, and that after sympathectomy the glycogenolytic reflex is not demonstrable in the muscle owing to the contrary effect of the sympathectomy on the muscle. This supposition is corroborated by the fact that the phosphagen content of the gastrocnemius muscle decreases after extirpation of the opposite gastrocnemius muscle, even when sympathectomy has been performed on the side of the remaining gastrocnemius muscle. In spasms from strychnine glycogenolysis is smaller in a muscle on the side on which a sympathectomy has been done than in a normal muscle.

After bilateral severance of the centripetal fibers from the hindlegs and unilateral sympathectomy, the glycogenolysis induced by strychnine poisoning on the side with remaining sympathetic nerves was even smaller than on the side of the sympathectomy. The authors assume that in strychnine intoxication the spasms of the skeletal muscles stimulate sensory endings in these muscles and that the impulses which are from here conducted toward the spinal cord stimulate sympathetic glycogenolytic centers. Proprioceptive reflexes seem to exist, which inform the central nervous system about the metabolism in single peripheral organs.

SPIEGEL, Philadelphia.

CLINICAL DIAGNOSIS OF DEMENTIA PARALYTICA IN MENTAL PATIENTS WITH A POSITIVE REACTION OF THE CEREBROSPINAL FLUID. C. E. ROBERTI, Riv. di pat. nerv. **41**:302 (March-April) 1933.

The author discusses the possibility that mental manifestations of the type of manic-depressive psychoses may occur in neurosyphilis with positive reactions of the cerebrospinal fluid. He thinks that in clinical cases of neurosyphilis in which mental deterioration is not present and in which the mental picture is one of a purely manic attack, the acute condition must be labeled as a syphilitic manic attack, an expression of a syphilitic psychosis but not necessarily of dementia paralytica. He thinks that if all syphilitic psychoses accompanied by positive serologic tests are labeled dementia paralytica, this is on the basis of a preconceived idea of the pathologic condition. Though it may happen that the manic attack is an expression of the constitutional tendency of the person with dementia paralytica and is therefore an initial clinical manifestation of otherwise typical dementia paralytica, the author thinks that there are cases in which the clinical manifestations of a manic attack occur in the presence of a positive reaction of the cerebrospinal fluid but in the absence of syphilitic lesions of the brain.

The clinical course of the disease is probably the only element available for a decision as to the real pathogenesis of the manic attack. Roberti, who does not seem optimistic as to the beneficial effect of malarial therapy, thinks that some

of the recoveries alleged as occurring in dementia paralytica may be recoveries from syphilitic psychoses with a positive Wassermann reaction which are not necessarily dementia paralytica. In the differential diagnosis between manic psychoses of a syphilitic nature and dementia paralytica he insists on the presence in dementia paralytica of a certain amount of mental deterioration that can be detected clinically.

FERRARO, New York.

CEREBRAL ARTERIES IN RELATION TO ARTERIOSCLEROSIS. C. R. TUTHILL, Arch. Path. **16**:453 (Oct.) 1933.

At the branching of large, and of many small, cerebral vessels are found areas of split elastic and collagen fibers which are present from birth and may remain unchanged through adult life. The onset of arteriosclerosis is an increase in the height and extension of these areas by collagen. Unless absorption of fat accompanies this growth of collagen, the areas are penetrated by split elastic fibers. The absorption of fat may be localized in only one hyperplastic area at the branching and in any part of such an area. Fat makes its first appearance in small globules in the fibers of collagen and in the bipolar fibroblasts. Fat cells are produced from the latter. A granulomatous formation occurs in a marked absorption of fat and cholesterol. In any absorption of fat, the collagen fibers are destroyed and also the elastic fibers, if present. Free lipoid accumulates from the destruction of the fat cells and this is followed by absorption of hyalin, cholesterol and calcium.

Arteriosclerosis may be rapid, slow or recurrent. Absorption of fat is marked in rapid growth and slight in slow growth. Recurrences may be of either rapid or slow growth and localized in the large or small vessels. Hypertension, disease, diet, volume of blood, lipoid metabolism, disturbed renal function and syphilis were considered in relation to arteriosclerosis. Neither age nor the wear and tear of vessels are an etiologic factor.

Macroscopic examination discloses arteriosclerosis only when there are either advanced regressive changes or a large amount of free lipoid from broken-down fat cells. Lesions of the media are apparently secondary to the changes in the intima. It is suggested that the primary hyperplasia of the areas at the branching is dependent on the volume of blood and that absorption of fat occurs as in tumor formations.

WINKELMAN, Philadelphia.

CHOLESTEROL: ITS RELATION TO MENTAL DISORDERS. A. GLEN DUNCAN, J. Ment. Sc. **79**:626, 1933.

Serum cholesterol is high in persons with dementia praecox who show passivity, dulness and apathy. When a dull patient becomes excited or agitated, the serum cholesterol is much lower. In affective psychoses, the cholesterol content is high during remission and decreases when the patient is manic or depressed. In epilepsy, the cholesterol content decreases when the patient is confused and occasionally during a convulsion. Increase in the emotional tone is associated with the fall of blood cholesterol, irrespective of mental disorder or whether the initial value is high or medium. It was previously observed that the blood cholesterol is high in myxedema and low or normal in exophthalmic goiter. The author postulates that there may be some relationship between a high cholesterol content and underactivity, and wonders what would happen if cholesterol should be given to an excited patient so as to increase the blood cholesterol. Conversely, would the decrease of the cholesterol content of the blood result in more activity? To twenty-four overactive and excited patients intramuscular injections of cholesterol in olive oil were given. In thirteen instances the injection of cholesterol was effective in reducing the excitement within a few hours. In eleven cases the injections had no effect. The solution was prepared by dissolving 1 Gm. of cholesterol in 20 cc. of olive oil which was sealed and sterilized in special ampules. The injections were given intramuscularly, the average dose being 1 Gm. In a previous series the

cholesterol content was reduced by giving the patients thyroid. The stuporous and semistuporous patients became more active and were stimulated for varying periods of time. The author believes that cholesterol is one of the controlling factors of cellular metabolism and that the central nervous system is susceptible to quantitative changes of this substance in its environment. KASANIN, Howard, R. I.

EFFECT OF HYPERTONIC DEXTROSE SOLUTIONS ON INTRACRANIAL PRESSURE IN ACUTE CRANIAL INJURIES. HARRY JACKSON ET AL., J. A. M. A. **100**:731 (March 11) 1933.

In order to determine accurately the efficacy of the intravenous injection of hypertonic dextrose solutions in acute cranial injury in man, Jackson and his associates used it in many cases and report their results in twenty clinical cases. In ten cases, 100 cc. of 50 per cent solution was used and, in ten cases, 200 cc. of 25 per cent solution. The solution was injected slowly during a period of from twenty-five to thirty minutes into the veins of the forearm. The results are summarized as follows: In eleven cases there was an initial drop in pressure of from 1 to 4 mm. of mercury during the first thirty minutes; then a gradual rise to a point above the initial pressure in two hours. In some cases this increase amounted to as much as 50 per cent of the original pressure. This was reduced to the initial pressure in twenty-four hours. In nine cases, however, the rise was immediate and continuous for two hours, with slight fluctuations, and gradually returned to the initial pressure in twenty-four hours. In about half the cases the blood pressure rose and the respiration became labored. This was more evident with the 50 per cent solution than when a 25 per cent solution was used, but it occurred with both. Headache was relieved for a short time in some cases, but not to the degree of relief obtained when spinal fluid was withdrawn, as was done in several cases. In normal animals used for experimental purposes, there is a primary fall in pressure because there is no hindrance to the circulation in the sinuses; the secondary rise in pressure is due to the absorption of dextrose by the brain cells and causes edema of the brain, but to a less extent than was found when sodium chloride was used. EDITOR'S ABSTRACT.

THROMBO-ANGIITIS OBLITERANS AMONG WOMEN. BAYARD T. HORTON and GEORGE E. BROWN, Arch. Int. Med. **50**: 884 (Dec.) 1932.

Thrombo-angiitis obliterans is rare among women; at the Mayo clinic there were seventy males for each female affected with this disease. In the literature, only seven instances of Buerger's disease among women have been previously reported; of these seven, Horton and Brown reject all but three. The present paper is a report of ten female patients suffering from thrombo-angiitis obliterans. The ages ranged from 30 to 71, the average being 39. In one case the race was not stated; of the remaining nine, three were classified as of American stock; one was Norwegian, one Dutch-English, one Scotch-Irish and three Jewish. Among the latter group the condition was more severe than among the remaining seven patients.

Of the various explanations to account for the relatively high incidence of this disorder among males, the authors are inclined to accept the hypothesis that the disease is usually milder among women and frequently unrecognized. In six of their ten cases, the disorder would have been overlooked by one not definitely searching for evidence of thrombo-angiitis obliterans. Other theories to account for the apparently sex-linked nature of the disease are: (1) that the vascular structures of males are naturally predisposed to disorder, as evidenced by the extent of coronary disease and arteriosclerosis among that sex; (2) that some focus of infection, such as the seminal vesicles, is usually at the root of the disease; (3) that there is an endocrinologic factor; (4) that tobacco is the basis of Buerger's disease. Evidence in support of these hypotheses is meager and inadequate, however, and Horton and Brown do not consider these explanations scientifically valid. DAVIDSON, Newark, N. J.

PERSISTENT DERMATITIS: UNUSUAL SEQUELA OF RADICAL OPERATION FOR TRIGEMINAL NEURALGIA. E. W. NETHERTON, J. A. M. A. **100**:722 (March 11) 1933.

The author reports the case of a married woman, aged 41, whom he has had under observation for a period of two years, and who acquired an unusual left-sided facial eruption following an operation on the gasserian ganglion. The eruption did not appear until one year following the operative procedure. The appearance of the eruption was that of a permanent flush with periodic exacerbations of an exudative inflammation. These exacerbations frequently followed exposure to heat, cold and wind and the use of soap and water, and, as would be expected, they were not accompanied by subjective symptoms. The patient was observed several times over a period of one year, and at no time was there involvement of the right side of the face. Likewise there were no vesicles suggestive of herpes. The patient had had attacks of urticaria and mild attacks of flexoral eczema, which antedated the operation for trigeminal neuralgia. Lack of cooperation prevented the author's complete investigation of this phase of her condition, but the nature of the lesion and its limitation made it seem unlikely that the dermatitis was the manifestation of an allergic state. A biopsy was not obtained. This request was not pressed because the patient was somewhat vindictive and refused to have any more operative procedures. The patient threatened to file a suit for malpractice because of the development of the dermatitis following the operation on the trigeminal nerve. This threat was not carried out, but it does suggest the possibility that such cases, in addition to their unusual clinical interest, may have some medicolegal significance.

EDITOR'S ABSTRACT.

BROMIDE INTOXICATION: ITS RELATION TO THE CONTENT OF BROMIDE IN THE BLOOD AND BARRIER PERMEABILITY TO BROMIDE. S. KATZENELBOGEN, H. GOLDSMITH and PAUL WHITE, Am. J. Psychiat. **13**:637 (Nov.) 1933.

There is no specific clinical syndrome on which a diagnosis of bromide intoxication can be based. The drug is usually given to neurotic or psychotic patients, and the symptoms of the intoxication bear the stamp of the patient's individual personality. The diagnosis depends on the detection of the salt in the blood. In a series of thirty cases, Katzenelbogen, Goldsmith and White found no constant relationship between the severity of the symptoms, the nature of the symptoms, the duration of the administration or the permeability quotient on one hand and the content of bromide in the blood on the other. The symptoms which they observed included abolition of the gag reflexes (ten cases), abolition of the abdominal reflexes (nine cases), acne and weakness (eight cases each), vertigo or unsteady gait (six cases) and, less commonly, nausea, anorexia, headache, somnolence and irritability. Delirium did not occur in any patient; however, the drug was not administered after clinical evidence of intolerance had developed. In most cases in which abnormal clinical symptoms occurred, the concentration of bromide in the blood was 250 mg. or more per hundred cubic centimeters. The authors suggest, therefore, that the drug be administered cautiously after this concentration has been reached. Many patients, however, had concentrations greater than this without clinical disturbances. The permeability quotient (blood to cerebrospinal fluid) bore no relationship to tolerance, so that the authors doubt if the clinical effectiveness of a drug used in neurologic conditions can be gaged by its tendency to diffuse into the spinal fluid.

DAVIDSON, Newark, N. J.

ON THE APPEARANCE OF INFILTRATIONS IN NEURASTHENIA AND THEIR SYMPTOMATIC AND THERAPEUTIC IMPORTANCE. A. HOFMAN-BANG, Acta psychiat. et neurol. **7**:233, 1932.

Subcutaneous and intramuscular infiltrations were found frequently in cases of classic neurasthenia, particularly among women. (They were present in 60 per cent of 85 neurasthenic patients and in 45 per cent of 35 nervous patients, but

in only 37 per cent of 161 patients suffering from other neurologic conditions. They occurred in 48 per cent of the female patients and 37 per cent of the male patients.) Similar infiltrations may be found in normal people, but they are not so easily produced nor do they give subjective symptoms. The author explains this by the fact that physiologic (vegetative) processes, which in well people go on without passing the barrier into consciousness, pass the barrier readily in neurasthenic persons. Also, the pressure of the infiltrations on the subcutaneous or intramuscular nerve endings more readily produces sensations in neurasthenic subjects. The infiltrations themselves perhaps are caused by a general asthenic condition which produces alterations in the liquid circulation and metabolic processes. Such infiltrations may be the organic basis for the so-called neurasthenic subjective symptoms. The author lists the various subjective symptoms—headache, vague pains, etc.—and cites the anatomic areas in which infiltrations can produce such symptoms. If this is the basis for the complaints, examination by palpation is necessary, and massage of the infiltrated areas becomes an important method of treatment. The author does state, however, that disappearance of the infiltrations is not necessarily accompanied by cure of the neurasthenia.

PEARSON, Philadelphia.

PREVENTION OF POLIOMYELITIS. SIMON FLEXNER, Brit. M. J. **1**:132 (Jan. 28) 1933.

Two important facts have been established in regard to poliomyelitis: (1) that the disease is a particular form of infection of the upper respiratory tract; and (2) that the cases arising during an epidemic cover a wide latitude in degree of symptoms and pathologic effects. There is evidence in support of the contention that slight cases express themselves as minor illnesses only, and their number may be many times greater than those with frank paralysis. Any degree of actual infection produces antiviral bodies in the blood, sufficient to protect monkeys inoculated with this disease. Monkeys are not naturally afflicted with poliomyelitis, as is man, and normal monkeys do not exhibit antiviral properties of the blood; even when they have recovered from the experimentally produced disease, their convalescent serum is less potent in antiviral activity than is human convalescent serum. Its potency can be increased, however, by the additional injection of virus into recovered monkeys. Previously it had been shown that the virus of poliomyelitis could be neutralized in a test tube by convalescent serum of both monkeys and man. Tests carried out by the author and his co-worker, Lewis, showed that this neutralization could also occur in monkeys in vivo. The results of these experiments showed, however, that the convalescent serum had no effect if introduced after paralytic symptoms had developed. Results of these experiments warrant a further and wider trial of this method of preventing epidemic poliomyelitis by immunization and also in the treatment of exposed persons before symptoms appear.

FERGUSON, Niagara Falls, N. Y.

SIGNIFICANCE OF DIRECT VENTRICULOGRAPHY FOR LOCALIZATION OF BRAIN TUMORS WITH SPECIAL REFERENCE TO TUMORS OF THE POSTERIOR FOSSA. F. HILPERT, Arch. f. Psychiat. **98**:388 (Dec.) 1932.

In an introduction Hilpert discusses the difficulties that are presented in clinical attempts at diagnosis of the localization of tumors of the brain in general, but especially of those of the posterior fossa. The effects of the general increase in pressure and remote effects of the tumor make it difficult to find any special set of symptoms that are pathognomonic for tumors of the posterior fossa. The most reliable symptoms are: (1) decrease of vestibular irritability; (2) compulsive postures of the head; (3) partial congestion syndromes which manifest themselves in positive Nonne-Apelt, Pandy and Weichbrodt reactions, normal cell count, and a mastic reaction of syphilitic type; (4) tachycardia in the presence of signs of increased intracranial pressure. But even these symptoms are not altogether

reliable, and Hilpert is of the opinion that the most important single diagnostic criterion is offered by direct ventriculography. This is to be preferred to encephalography because the results are better and there is less danger in tumors of this type.

Twenty-six cases are reported in which direct ventriculography was undertaken; in most of them the results were highly satisfactory. The author describes the technic that he uses; he is of the opinion that the amount of air injected does not have any essential influence on the results, but that the most favorable pictures were obtained when the amount of air injected was four fifths that of the fluid withdrawn.

MALAMUD, Iowa City.

THE ELIMINATION OF BROMIDES FROM THE BLOOD STREAM. J. W. PALMER and H. T. CLARKE, J. Biol. Chem. **99**:435 (Jan.) 1933.

The authors, in their first experiment, studied the halide content of the blood and the urine of a dog for a period of four and one-half months after the intravenous injection of sodium bromide. Thirty minutes after the injection, the blood contained nearly 15 millimols of bromide per liter; four and one-half months later, there was still 2 millimols per liter. During the first day after the dose of bromide, the increase in excretion of chloride was molecularly equivalent to 80 per cent of the bromide given, while the bromide excretion was 8.6 per cent. After the first day, the ratio of the fraction of bromide in total halide in the blood plasma to that in the urine is constant during the constant intake of chloride. The kidneys then excrete chloride preferentially over bromide. In the second experiment bromide was give by mouth. After the first day there was the same constancy of the ratio of the fraction of bromide in total halides in plasma to those in urine. In a third experiment, after the injection of bromide, the excretion of bromide increased immediately after the dose of chloride. The effect subsided as soon as the excess chloride was eliminated. In a control experiment urea was also given, causing diuresis as sodium chloride does, but the increase in urinary volume did not affect the amount of chloride or bromide excreted or the ratio. In the treatment of bromism the supply of chloride is important, for it not only increases the halide excretion but increases the fraction of bromide in it.

DAILEY, Boston.

SYNDROME OF CLAUDE-BERNARD-HORNER CAUSED BY A PARAGANGLION CAROTICUM OVERLYING THE CAROTID ARTERY. E. PUSCARIU and D. LAZARESCO, Ann. d'ocul. **170**:350 (April) 1933.

Puscariu and Lazaresco report the following case: G. C., aged 41, who was examined in 1921, presented a slightly moveable, painless, deeply situated growth in the right cervical region, the size of a hazelnut. In 1926, the tumor began to increase rapidly in size and to transmit pulsations of the carotid artery, and slight ptosis appeared on the right side. In July, 1930, the patient entered the Iassy clinic, where the following report was made: slight ptosis on the right side; palpebral fissures: right, 4 mm.; left, 7 mm.; right pupil, 3 mm. in diameter, left, 4.5 mm.; right enophthalmos, 11 mm., left, 12; pupillary reflexes normal on both sides; normal vision in each eye; tension, right, 19 mm., left, 23 mm.; no hyperemia of the conjunctiva, choroid or retina; fundus normal; normal lacrimal secretion; right nasal hypersecretion; no heterochromia of the iris, and normal accommodation. Instillation of cocaine produced dilation of the left iris, but no modification of the right iris. Instillation of epinephrine produced bilateral mydriasis. The heart, lungs and Bordet-Wassermann reaction were normal; the blood pressure was 110 systolic, and 70 diastolic. The tumor was extirpated by M. Hortolomei. Microscopic examination revealed the structure of a paraganglion, with large areas having the structure of a cavernous hemangioma. Two months later, the ocular phenomena still persisted and hypotonia was present.

BERENS, New York.

SPINAL FLUID CELL COUNT AND ENCAPSULATION OF BRAIN ABSCESS: ATTEMPT TO CORRELATE THESE FACTORS AND TO DETERMINE OPTIMAL TIME FOR DRAINAGE. H. W. WOLTMAN, J. A. M. A. **100**:720 (March 11) 1933.

The author states that abscess of the brain presents a highly varied clinical panorama that cannot be reduced to a simple formula. Each case is a law unto itself. The problem calls not only for a diagnosis but also for a decision as to when the abscess shall be drained. Awaiting the optimal time means a better capsule and a liquefied interior, and consequently better drainage; it means less virulent organisms and greater immunity, and hence less danger to the patient. The risk of performing spinal puncture in cases of abscess has probably been overrated, and thus physicians have been deprived of information that might be helpful. After invasion of the brain has taken place and the formation of an abscess gets under way, the number of neutrophils in the spinal fluid becomes absolutely and relatively reduced. The persistence or reappearance of neutrophils suggests that encapsulation is not progressing favorably. An appreciable number of neutrophils may indicate extension of the abscess or close proximity of the abscess to the ventricle. A predominance of neutrophils in the spinal fluid was seen in cases in which operation was performed unnecessarily or which ended fatally. A small number of lymphocytes would seem, on the whole, to indicate better encapsulation, greater resistance and a smoother convalescence after operation.

EDITOR'S ABSTRACT.

IDIOPATHIC OSTEOPSATHYROSIS OR LOBSTEIN'S DISEASE IN AN EPILEPTIC SUBJECT. JACOPO NARDI, Riv. di pat. nerv. **41**:1 (Jan.-Feb.) 1933.

Nardi reports a case of osteopsathyrosis in an epileptic patient. He reviews the literature on spontaneous fractures of bones in mental diseases, particularly in epilepsies, and the diverse hypotheses as to their pathogenesis, citing various evidences of the importance of hormonal factors in osteogenesis and in bone dystrophies. He suggests that osteopsathyrosis may be due to an altered calcium metabolism related to dysfunction of the anterior lobe of the pituitary gland or of the diencephalic pituitary region. Because epilepsy may also be related to endocrine dysfunction, he outlines the possibility of a so-called pituitary epilepsy. His conception is supported by the hypocalcemia which exists concomitantly in cases of hypofunction of the prehypophysis and the frequency of convulsive manifestations associated with other changes in the bony skeleton in cases of hyperfunction of the pituitary gland. It follows that convulsive manifestations may be present in both hypofunction and hyperfunction of the pituitary gland in relation to a modified calcium metabolism. The coexistence of the two syndromes in the same patient leads the author to establish in the case which he reports a common ground for the osteopsathyrosis and the epilepsy, grounds represented by a modified calcium metabolism of diencephalic pituitary origin.

FERRARO, New York.

SPONTANEOUS SUBARACHNOID HAEMORRHAGE OF INTRASPINAL ORIGIN. H. DOUGLAS-WILSON, SINCLAIR MILLER and GEORGE W. WATSON, Brit. M. J. **1**:554 (April 1) 1933.

Spontaneous subarachnoid hemorrhage of cerebral origin occurs with moderate frequency. The onset is usually sudden, generally with loss of consciousness, which passes off gradually. It is followed by severe headache, often in the occipital region, accompanied by recurrent vomiting and more or less confusion. As a rule there is no paralysis or sensory changes. The fundi may show retinal hemorrhage, or there may be only a papillitis. On lumbar puncture the cerebrospinal fluid is usually under slightly increased pressure and contains blood. The number of recoveries more than outnumber the deaths. If the patient survives, there are, as a rule, no sequelae. Spontaneous subarachnoid hemorrhage of intraspinal origin is much rarer.

A case illustrating the latter condition is reported. It is that of a man aged 40. The outstanding signs and symptoms included: almost complete absence of cerebral symptoms at the onset; severe pain in the lumbar region, excruciating at times and increased by movement; rigidity of the spine, with a mild degree of opisthotonos; marked irritability and hyperesthesia of the spinal roots and nerves and the almost instantaneous relief from symptoms on lumbar puncture. It would appear that in this case hemorrhage occurred on four separate occasions. Its cause is unknown.

FERGUSON, Niagara Falls, N. Y.

THE SPECIFIC DYNAMIC ACTION OF PROTEIN IN PATIENTS WITH PITUITARY DISEASE. MARSHALL N. FULTON and HARVEY CUSHING, Arch. Int. Med. **50**:649 (Nov.) 1932.

In view of the reports of many foreign investigators that in pituitary disease the specific dynamic action of protein is suspended, Fulton and Cushing conducted a study on the effect of protein on metabolism. Their material consisted of eighty-four patients divided into five groups according to the type of pituitary disease. Each patient received a basal metabolic test fourteen hours after his last meal. Following this, 200 Gm. of broiled chopped beef was administered, with which 100 cc. of water was allowed. Metabolic determinations were then made every hour for four hours following the meal. The number of patients in each group and the average rise in metabolism following the meal were: (*a*) Fourteen patients with frank acromegaly showed an average rise of 19 per cent; (*b*) seven with fugitive acromegaly, a rise of 18 per cent; (*c*) thirty-two with pituitary insufficiency and chromophobe adenoma, a rise of 23 per cent; (*d*) sixteen with nonadenomatous tumors secondarily affecting the hypophysis, a rise of 20 per cent, and (*e*) a control group of thirteen patients with tumors not in juxtaposition to the gland, a rise of 23 per cent. The average metabolic rise for the entire series was 20.7 per cent. These responses were all within normal limits, lending support to the view that the endocrine glands have no direct bearing on the specific dynamic action of food.

DAVIDSON, Newark, N. J.

BRAIN TRANSPLANTATION IN REGENERATING EARTHWORMS. BENJAMIN KROPP, J. Exper. Zool. **65**:107 (April 5) 1933.

Earthworms (Helodrilus caliginosus Sav.) were decapitated by the removal of five segments from the anterior end. The injection of suspensions of fresh or dried macerated ventral nerve cord or brain into the regenerating end of the worms had no effect on the rate or manner of regeneration. The removal of ten segments of ventral nerve cord from a decapitated worm only retarded regeneration. A new head was formed, and connection was secondarily established between the regenerated nervous system in the head and the forward-growing ventral nerve cord.

A brain transplanted to the dorsal side of the first or second remaining segment of a decapitated earthworm established no nervous connections with the nerve cord. The transplanted brain became surrounded by connective tissue and was gradually resorbed. A brain transplanted to the ventral side of the decapitated worm and placed in contact with the cut end of the ventral nerve cord, or close to it, established immediate and intimate nervous connections with it. It is concluded that the nervous system of the earthworm has no determinable functional relation with the phenomenon of regeneration of the head. Within the limits of the experimental procedure used, no active substances associated with regeneration of the head in the earthworm could be recognized.

WYMAN, Boston.

BLOOD CHOLESTEROL IN THYROID DISEASE: II. EFFECT OF TREATMENT. LEWIS M. HURXTHAL, Arch. Int. Med. **52**:86 (July) 1933.

The average blood cholesterol (in milligrams per hundred cubic centimeters) in thirty-four patients with exophthalmic goiter who had had no iodine treatment

was 123. After a course of treatment with compound solution of iodine, this had risen to 144 mg. The corresponding figures in patients with toxic adenomatous goiter were 132 and 160 mg. In a group of twenty-five patients the average preoperative content was 146; a week after subtotal thyroidectomy the cholesterol index was 154; three months later, 169; a year later, 167. It would appear that both iodine therapy and operation were capable of elevating the abnormally low cholesterol content in these cases. A definite but limited value may be attached to the cholesterol determination in cases of thyroid disease. Those more severely affected show the lowest indexes; a reciprocal relationship apparently exists between the elevation of the basal metabolic rate and the amount of cholesterol in the blood. In instances of toxic goiter, in the absence of complicating acute infection, a figure below 100 mg. cholesterol per hundred cubic centimeters of blood suggests a severe degree of toxicity. On the other hand, amounts in excess of 180 point to the mildness of the thyrotoxicosis. Patients showing more than 200 mg. (unless during a remission) are probably not suffering from hyperthyroidism at all.

DAVIDSON, Newark, N. J.

THE ACTION OF PITUITARY POSTERIOR LOBE EXTRACTS ON DIFFERENT PARTS OF THE CIRCULATORY SYSTEM. PETER HOLTZ, J. Physiol. **67**:149 (Oct. 4) 1932.

This paper is an attempt to explain the effect of preparations of the pituitary gland on the circulation, by describing first, investigations on anesthetized but otherwise intact animals, and second, experiments on isolated tissues of perfused organs in order to analyze the results obtained on the whole animal. The effects seen in different species of animals were compared in order to gain a wider basis on which to criticize the results. Commercial extracts, the complete extract as well as the separated pressor and oxytocic principles, were all used in different parts of the investigation. Holtz found that pituitary extracts have no action on the pulmonary vessels. Either the complete extract or the separated pressor fraction produces a rise of pressure in the pulmonary artery of the cat, which is secondary to an increase of pulmonary flow. They produce a fall of pulmonary arterial pressure in the rabbit and in the dog, which is due to a diminution in coronary flow. An additional cause of this fall in the dog is the accumulation of blood in the splanchnic area. Pituitary extracts cause a fall of pressure in the portal vein of both the cat and the dog. In the cat, this is due to selective constriction of the mesenteric arteries and to constriction of the hepatic artery. In the dog it is caused mainly by dilatation of the hepatic veins. This is due to the content of oxytocic substance of the extracts.

ALPERS, Philadelphia.

DIATHERMY IN THE TREATMENT OF GENERAL PARESIS. HUGH MCKAY, KENNETH GRAY and WILLIAM WINANS, Am. J. Psychiat. **12**:531 (Nov.) 1932.

Since it is generally accepted that the high temperature rather than any specific biochemical reaction is responsible for the success of the fever treatment of dementia paralytica, the diathermy machine, more readily controlled than a malarial infection, will become increasingly useful in the treatment of that disease. The authors report the results in twenty-eight patients who had received diathermy accompanied by neoarsphenamine and bismuth preparations. The former is given in weekly intravenous treatments, the dosage being gradually increased from 0.45 to 0.75 Gm. Bismuth is administered intramuscularly. The diathermy treatments are given on alternate days, the Victor superpower machine being used. The current level is from 4 to 6 amperes; a half hour is required to step up the current intensity to the proper level. In about three hours the patient's temperature rises to 104 F., and the current is then turned off. Of the twenty-eight patients, eleven had complete or almost complete remissions, seven had partial remissions, seven were unimproved, and three died. Of the latter, one died of pneumonia,

one of hemiplegia and one of hyperpyrexia. The last patient appears to have been unduly susceptible to the influence of high temperatures. In nineteen of the cases no change in the spinal fluid was noted after treatment. In six patients, the colloidal gold curves became normal.

DAVIDSON, Newark, N. J.

EFFECTS OF GLYCINE (GLYCOCOLL) IN MUSCULAR DYSTROPHY WITH ESPECIAL REFERENCE TO CHANGES IN STRUCTURE AND COMPOSITION OF VOLUNTARY MUSCLE. J. G. REINHOLD, J. H. CLARK, G. R. KINGSLEY, R. P. CUSTER and J. W. MCCONNELL, J. A. M. A. **102**:261 (Jan. 27) 1934.

The authors studied the effects of glycine in nine cases of progressive muscular dystrophy for periods up to fourteen months. Little tangible evidence of improvement in muscular function was obtained. Specimens of muscle for biopsy removed after treatment were distinctly better in quality, chemically and histologically, than similar specimens taken before treatment. Restoration of various characteristic muscle components accompanied regeneration of the muscle fibers. Diets high in protein, beef extract and gelatin proved to be helpful supplements to glycine. Ephedrine was of value in one case. A patient with generalized chronic myositis that closely simulated the clinical picture of muscular dystrophy showed considerably improved muscular function following glycine therapy. Despite the marked improvement in the structure and composition of the muscles in progressive muscular dystrophy after treatment with glycine (as indicated by biopsy), a great disparity with the normal remained, probably sufficient in many cases to account for the failure of muscular function to be restored to a greater extent. The possibility of inducing further regeneration, perhaps sufficient to bring about unquestioned clinical improvement, remains to be tested.

EDITOR'S ABSTRACT.

RETROBULBAR NEURITIS AND DIPLOPIA, WITH SIGNS OF FRONTAL SINUSITIS: OPERATION; ABSENCE OF SINUSITIS; RECOVERY. J. SOUCHET and A. LACROIX, Rev. d'oto-neuro-opht. **11**:26 (Jan.) 1933.

This observation concerned a woman, aged 52, who, following a slight coryza, suffered violent pain in the left supra-orbital region, accompanied by exquisite tenderness over the outer part of the frontal sinus area in the forehead and in the orbit. A roentgenogram revealed cloudiness over the left frontal sinus, more marked over the lateral part and extending beyond its boundary, and cloudiness of the left maxillary sinus. Examination of the eyes showed diplopia, limitation of movements, a small central scotoma for colors, a contracted visual field and a visual acuity of 1/10 in the left eye. Opening of the sinus revealed an apparently normal cavity. Relief from pain was prompt, and vision rapidly became normal, although a transitory spasmodic myopia occurred in both eyes during convalescence. Punctures of the left maxillary sinus gave negative results. The tenderness over the forehead is explained by periostitis, and it is assumed that the origin of the retrobulbar neuritis was the coryza, the infection passing over the sinus itself and attacking the surrounding periosteum and dura. From this point it could readily reach the optic nerve by means of the cellular tissue. In 1921, Lemaitre thought that many cases of retrobulbar neuritis arose in this manner. The entire question is still too vague to permit of more than an expression of opinion.

DENNIS, Colorado Springs, Colo.

THE DIFFERENTIAL EFFECTS OF ARSPHENAMINE AND TRYPARSAMIDE. H. C. SOLOMON, S. H. EPSTEIN and A. BERK, Am. J. Syph. **17**:45 (Jan.) 1933.

That arsphenamine has a high therapeutic index as measured by its effects on the Spirochaeta pallida is well known. On the other hand, its inferiority to tryparsamide in the therapy of neurosyphilis is generally recognized. This cannot be explained adequately by the side-chain theory of Ehrlich, nor will the assumption that the hemato-encephalic barrier obstructs the passage of the large molecule of arsenic explain the difference in the action of these drugs. By comparing the

effects of these preparations on rat-bite fever (sodoku) the authors are able to demonstrate a significant differentiation. Rat-bite fever is caused by the Spirochaeta morsus-muris and bears a close clinical resemblance to syphilis. Arsphenamine seems to cure this disease, whereas tryparsamide causes involution of the primary sore but is without effect on the fever or on the rash. The open lesion is apparently stimulated to rapid repair by tryparsamide, whereas the organism is unaffected. In malaria a similar process is noted. Arsphenamine stops the fever by destroying the plasmodia; tryparsamide, on the other hand, has no such effect. The authors conclude, therefore, that the beneficial effects of tryparsamide in neurosyphilis are due to local action in specific areas within the nervous system, rather than to any spirocheticidal action. DAVIDSON, Newark, N. J.

TUMORS OF THE GASSERIAN GANGLION. MELBOURNE J. COOPER, Am. J. M. Sc. **185**:315 (March) 1933.

A total of only seventy-six cases of tumors of the gasserian ganglion is reported in the literature, and in surgical observations they are relatively rare. The author reports three cases of tumor primary in the region of the gasserian ganglion. From an analysis of twenty-two case reports, the clinical picture is characterized by an initial symptom such as pain in some part of the trigeminal distribution, subjective numbness in that area, impairment of vision or hearing, nausea, vertigo or headache; by an objective finding such as trigeminal sensory impairment or hyperesthesia, diminution of the corneal reflex or weakness of the motor division, or by a combination of more than one of these manifestations. Almost 50 per cent of the pathologic diagnoses were endotheliomas. In patients who suffer constant trigeminal pain unsatisfactorily explained and show signs of involvement of the trigeminal nerve without evidence of an etiology other than tumor of the ganglion, exploratory operation is justified. MICHAELS, Boston.

CEREBROMACULAR DEGENERATION. E. D. MACNAMARA, W. E. CARNEGIE DICKSON and T. R. HILL, J. Neurol. & Psychopath. **13**:211 (Jan.) 1933.

A case of so-called cerebromacular degeneration in a non-Jewish child, aged 6, is reported with a pathologic investigation. The onset occurred at 3 years with a convulsion. Ataxia of gait, progressive muscular weakness and impairment of vision and mentality set in. Neurologic examination revealed optic atrophy, without a cherry-red macular spot, jerky movements, and a bilateral Babinski sign with increasing spasticity. Throughout the brain and cord there were fatty degenerative changes in the nerve cells. Widespread demyelinization of the white nerve fibers of the cerebrum, cerebellum and brain stem was present. The spinal cord changes were less marked than those of the brain. The authors believe that this case has the characteristics of Tay-Sachs' disease, but they failed to find evidence in the examination of the liver to support the theory that it is related to Gaucher's or Niemann-Pick's disease, that it is a form of general lipoid degeneration. No references are given in the article. SPERLING, Philadelphia.

ON POSTURE AND POSTURAL REFLEX ACTION: THE EFFECT OF UNILATERAL LUMBAR SYMPATHETIC CHAIN EXTIRPATION. GILBERT PHILLIPS, Brain **54**: 320 (Sept.) 1931.

In decerebrate cats, the left lumbar sympathetic chain having been removed, the left leg would not support the weight of the caudal end of the trunk, whereas the right leg did. Lengthening and shortening reactions were constantly present in the vastocrureus muscles of both sides, as were also the crossed extensor reflexes. Decerebrate rigidity develops and is maintained in the left hindlimb of decerebrate cats after removal of the left lumbar sympathetic chain, so that the postganglionic fibers of the sympathetic nervous system do not constitute the efferent limb of the reflex arc subserving posture in skeletal muscle. The excitability of the proprio-

ceptive nerve endings situated in the left vastocrureus muscle has been enhanced by the special sympathectomy. All changes in postural tonus following sympathetic extirpation appear to be quantitative rather than qualitative.

MICHAELS, Boston.

SPINAL GANGLION RESPONSES TO THE TRANSPLANTATION OF LIMBS AFTER METAMORPHOSIS IN AMBLYSTOMA PUNCTATUM. R. L. CARPENTER, J. Exper. Zool. **64**:287 (Jan. 5) 1933.

A method is described for grafting limbs on the young of Amblystoma after metamorphosis. Nineteen heterotopic forelimb grafts were made on animals from 46 mm. to 109 mm. in length and from nine to three hundred and seven days after metamorphosis. Three successful cases and one case of regeneration of a limb from tissue remaining after the graft had degenerated were obtained. In the three successful ones, each of the grafted limbs received its innervation from a single spinal nerve. The spinal ganglia of these nerves underwent hyperplasia of from 16 to 27 per cent in response to the increase of their peripheral fields. In comparison with cases in which the operation was performed during larval life, these showed the sensory hyperplasia to be considerably reduced, especially since the peripheral overload was centered entirely on a single spinal nerve.

WYMAN, Boston.

FOCAL INFECTIONS IMPLICATING THE NERVOUS SYSTEM. FOSTER KENNEDY, Am. J. M. Sc. **185**:305 (March) 1933.

Numerous cases are presented to show the prevalence of neural complications of focal infection. In 182 cases of acute follicular tonsillitis, 9.9 per cent of the patients had severe referred pain as a prominent symptom. In 294 cases of nasopharyngeal-laryngeal diphtheria in which the patients were treated with antitoxin, 4.4 per cent showed involvement of the nervous system. An important conclusion of Walshe was that invariably there was an initial local paresis related anatomically to the site of the infected focus in cases of so-called desert-sores with Klebs-Löffler bacilli. In 765 cases diagnosed as neuritis (but not including polyneuritis), about 1 per cent of the patients manifested severe cauda equina neuritis. Of 137 cases of transverse myelitis, 5.1 per cent were secondary to a known infection. Of 422 cases of meningitis, 5.7 per cent followed infections about the head. The details of the cases are presented in chart form.

MICHAELS, Boston.

STUDIES OF VISUAL FIELDS IN FUNCTIONAL HEADACHES OF PITUITARY ORIGIN. BEULAH CUSHMAN, J. A. M. A. **101**:837 (Sept. 9) 1933.

While making a study of headaches which had been treated in the past six years by means of the roentgen rays and glandular extracts, Cushman noticed striking similarities of the visual fields. In a few cases in which correction of the refractive error did not relieve the cephalalgia, a study made with the aid of the internist, the roentgenologist and visual fields led to the belief that these headaches are of pituitary origin. From this study, the author concludes that certain periodic attacks of headaches and discomfort of the eyes simulating ciliary spasm may be due to dysfunction of the organically sound pituitary gland or to distention of its capsule by physiologic hypertrophy. The majority of the visual fields show a contraction of the superior temporal quadrant for color and varying changes in the form fields.

EDITOR'S ABSTRACT.

THE ARSPHENAMINES AS A FACTOR IN THE PRODUCTION OF NEUROSYPHILIS. PAUL O'LEARY and JAMES R. ROGIN, Arch. Dermat. & Syph. **26**:783 (Nov.) 1932.

Finger, Fraser, McDonagh and others have maintained that the affinity of the arsenical drugs for the nervous system might result in the development of neuro-

syphilis in patients treated with arsphenamine derivatives. This contention is not borne out by the studies of O'Leary and Rogin. Their material consisted of 500 patients with syphilis of the central nervous system, 85 per cent of whom had had no previous treatment with arsenical preparations of any sort. The remaining 15 per cent had received arsphenamine, but the therapy had been adequate in only a fifth of them. It would appear, therefore, that the more serious type of involvement was much commoner in cases in which arsphenamine had not been given than in those in which arsenical treatment had been received.

DAVIDSON, Newark, N. J.

EFFECT OF VEGETATIVE DRUGS ON FAT METABOLISM. A. LÁNCZOS, Arch. f. d. ges. Physiol. **231**:571, 1933.

The fat content of the liver is usually lowered by injections of pilocarpine, but is increased in the springtime, as shown by experiments on mice. This variation in effect is explained by the different action of the drug on the temperature of the body. In winter and summer pilocarpine produces a marked fall of body temperature; in spring it causes only a very slight hypothermia. A decrease of the fat in the liver was found only when the hypothermia was marked and lasted for several hours. The return of normal temperature was associated with an increase of the fat in the liver.

RETROGRADE CHANGES IN HUMAN SENSORY NERVES AFTER INJURIES TO THE NERVE TRUNKS. F. SCHULZ, Arch. f. d. ges. Physiol. **231**:708, 1933.

Schulz experimented with his own nervi cutanei antebrachii mediales et laterales. After injuries to these nerves (severing, freezing and slight mechanical irritation after exposure), he found regularly a decrease of the rheobases and a lengthening of the chronaxia in the sensory nerve central to the injury. In a control experiment an incision into the skin was made without touching the nerve. This increased the rheobase. After the nerve had been frozen twice, its function returned in eight days

ELECTRIC STIMULATION OF A SINGLE MOTOR NERVE FIBER. S. SAKAMOTO, Arch. f. d. ges. Physiol. **231**:489, 1933.

Sakamoto uses a micro-electrode to stimulate motor nerves in frogs. The electrode allows the stimulation of single fibers. The relation between the intensity and the duration of the stimulus follows the law of Weiss (hyperbolic form of the curve) as long as single fibers are stimulated. The chronaxia varies rather much in the same muscle (from 0.047 to 0.316 per millisecond).

THE CONDITIONED REFLEXES OF DOGS AFTER EXTIRPATION OF THE PITUITARY GLAND. W. J. KRIASCHEW, Arch. f. d. ges. Physiol. **232**:389, 1933.

The behavior of dogs after extirpation of the pituitary gland shows infantile traits. Kriaschew observed a loss of specific reflexes (e. g., the sexual reflex). The threshold for electric stimulation of the skin is lowered. The irradiation of the excitation in the conditioned defense reaction is lowered; the general motor reaction is followed by inhibition immediately after the stimulus subsides. The local conditioned motor reflex of the paw expires much earlier than in normal animals.

THE HUMORAL TRANSMISSION OF EXCITATION FROM ONE NEURON TO ANOTHER. A. W. KIBJAKOW, Arch. f. d. ges. Physiol. **232**:432, 1933.

The author stimulated the cervical sympathetic trunk to see whether such stimulation produces chemical substances in the upper cervical ganglion which have a stimulating effect on the nerve cells of this ganglion. He perfused the

ganglion with Ringer-Locke's solution and collected the fluid after it had flowed through the ganglion. The fluid collected during stimulation of the cervical sympathetic trunk was able to stimulate the cells of the upper cervical ganglion, as shown by the contraction of the nictitating membrane.

THE INFLUENCE OF LIGHT ON THE ACTIVITY OF THE PITUITARY GLAND IN FROGS. G. KOLLER and W. RODEWALD, Arch. f. d. ges. Physiol. **232**:637, 1933.

Extracts of the pituitary gland from frogs which are kept in the dark for from three to twenty minutes do not expand the melanophores. Exposure of the frogs to daylight (15 seconds in the spring) is sufficient to restore this quality of the pituitary gland. This reflex influence of the light on the pituitary gland is due to stimulation of the retina. Mechanical stimulation of the optic nerve has the same effect.

OBSERVATION OF THE CUPOLA IN THE AMPULLAE OF THE PIKE'S LABYRINTH. W. STEINHAUSEN, Arch. f. d. ges. Physiol. **232**:500, 1933.

The cupola was stained with Chinese ink and observed in living pike. Electric stimulation produced typical labyrinthine symptoms without movements of the cupola. Deviation of the cupola in the left horizontal ampulla was induced by mechanical stimulation. Short deviation of the cupola toward the utriculus produced deviation of both eyes to the right; prolonged deviation caused nystagmus to the left. Deviation of the cupola toward the semicircular canal had no effect.

LABYRINTH REFLEXES IN GUINEA-PIGS AFTER REMOVAL OF THE OTOLITHS BY CENTRIFUGATION. A. DEKLEYN and C. VERSTEEGH, Arch. f. d. ges. Physiol. **232**:454, 1933.

Tonic labyrinth reflexes can still be elicited after complete separation of the otolith membranes with the maculae. These reflexes seem to start from the maculae utriculi. The reactions on rectilinear movements are also still present; they are probably a function of the semicircular canals.

SPIEGEL, Philadelphia.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Joint Meeting, March 6, 1934

CLARENCE P. OBERDORF, M.D., *Chairman, Presiding*

RESULTS OF MUSCLE TRAINING IN (A) ANTERIOR POLIOMYELITIS; (B) SPASTIC HEMIPLEGIA; (C) CHOREA AND HABIT MOVEMENTS: CASE PRESENTATIONS. DR. MORRIS GROSSMAN.

Many disorders of the central nervous system are characterized by disturbance in the control of the limbs because of a flaccid or spastic paralysis. It has long been recognized that there is a psychologic as well as a physiologic element in most symptoms, especially those associated with a disability which may result in partial or complete immobilization, such as poliomyelitis, hemiplegia or tabes dorsalis. The mental state of these patients is an important factor in their care and in the ultimate outcome of the case. To meet the requirements of life with such a disability as exists in tabes or hemiplegia requires herculean efforts on the part of the patient. Maximal efforts produce only minimal results in function. This not only causes extreme fatigue but tends to intensify the already existing disturbed mental state of the victim, and frequently irritability and depression add to the misery. Fear complexes readily form, and as they become elaborated they produce an unrelieved state of mental perturbation. With the use of breathing and rest exercises these mental states can be successfully combated and largely avoided. It is unfortunately too true that many patients are not considered sufficiently from the standpoint of treatment but are regarded mostly from the standpoint of diagnosis, and are often left to their own devices for the care of their disability, or at best are relegated to the care of lay persons practicing massage or physical therapy, many of whom have no conception of the physiologic or psychologic problems that must be solved for successful treatment.

Every patient with a flaccid or a spastic type of paralysis must be carefully guarded against the possible formation of contractures, which invariably occur when reciprocal muscle action is disturbed. Periarthritic changes due to immobilization must also be avoided if possible. The early use of splints, passive movements at the various joints and the awareness that they are always liable to occur will usually be sufficient to prevent these painful complications.

The use of mechanical measures as temporary aids in the treatment of the paralysis in hemiplegia and poliomyelitis is indicated in many cases. Corrective shoes are of great value in cases of hemiplegia and for the hypotonic tabetic foot. Modified Whitman plates, made from models of casts taken of the foot at rest and when bearing the body weight, are also of service in correcting the deformities of the foot in tabes. However, the most important element in the correction of these paralytic states and disturbances in coordinated movements is the persistent and patient application of muscle training.

The method of reeducation that has been most successful in my hands is adapted from that advocated by Dr. William J. M. A. Maloney for the cure of ataxia, described in the *New York Medical Journal* (**98**:1045 [Nov. 29] 1913). The exercises may be divided into three groups: (1) breathing, (2) relaxation and (3) muscle training. The diaphragmatic type of breathing is used. The patient is put in a recumbent position, and a sandbag is placed on the abdomen; he is

asked to breathe deeply, moving the sandbag slowly up and down; thoracic movements are restricted. A slight pause at the end of each inspiration and expiration is taken. The patient next passes to breathing of moderate amplitude and later to gentle breathing.

When the breathing has become slow and regular, relaxation of the muscles is begun. To induce it, passive movements are employed. The muscles about a joint are alternately lengthened and shortened, and the patient is directed to feel the difference in the tension of the muscles when they are relaxed. As soon as the muscles of one joint are under control, the next joint of the same extremity should be similarly manipulated, until the entire limb lies flaccid and falls limply from any unsupported position. Each extremity is dealt with independently.

Movements are then begun. At first only the simplest movements should be taught. The beginning and the end of a movement should be fixed. To define the direction and extent of the movement, it is first passively performed by the physician. Then the patient resists this passive movement. Next the patient attempts to perform the movement guided by the operator, guidance being gradually diminished as the movement is more accurately performed. Finally, the movement is repeated against resistance. For rhythm and rate, a metronome can be used. As the simple movements are perfected, more complicated ones at several joints are attempted. When the patient is able to perform all of the exercises properly in the recumbent position, similar ones are given at first in the sitting position and later, after he is able to balance well, in the upright position. Finally, he repeats the exercises while moving backward, forward and from side to side. Each step must be thoroughly mastered before any advance in the exercises is attempted.

The following cases of poliomyelitis, hemiplegia, chorea and tic will illustrate some of the results which can be obtained with persistent muscle training supplemented by the various mechanical measures previously outlined.

CASE 1.—C. G., a schoolgirl, aged 17, had had an attack of acute anterior poliomyelitis about eighteen months ago with complete flaccid paralysis of all extremities and loss of all superficial and deep reflexes. The muscles of the back and shoulders and the intercostal and abdominal muscles were markedly weakened. The irritative stage lasted about four weeks, during which the extremities were kept in position with sandbags. Boards were used under the mattress to keep the back up, and a cushion was placed between the shoulder blades. As soon as the irritative stage was over, passive movements were begun; to these were added active movements of muscles showing recovery of power. Each muscle was given a little passive movement daily. Soon it was evident that some of the muscles would regain power more rapidly than others; efforts were concentrated on them until definite function was reestablished. The muscles of the left shoulder, arm and leg, with the exception of the triceps and the flexors and extensors of the fingers, recovered first. The muscles of the back and shoulder next regained strength to the point where the patient was able to maintain a sitting posture with support. In four months she was able to sit out of bed for short periods. Standing with support was next attempted, and walking with support soon followed. Last summer swimming was resumed. The patient had been an excellent swimmer, and soon began to swim fairly well. Improvement on the right side has been slower. Power is returning in the right deltoid and biceps muscles and in the left triceps. The patient is now able to walk, dance, swim and attend courses in college, handicapped only by the lack of finer movements of the hands, which are slowest to recover.

CASE 2.—F. S., a housewife, aged 41, about two years ago awoke one morning with hemiplegia. After five weeks she had improved sufficiently to leave bed. I saw her nine months later. Neurologic examination showed moderate vascular hypertension and marked left spastic hemiplegia. The left shoulder could scarcely be moved because of periarthric changes. Gait was much impeded because of contractures and marked spasticity. Exercises were begun but were discontinued after a few weeks. Treatment was resumed one year later. During the interval she

had exercised a little from time to time but with no regularity. Her condition was somewhat improved. Regular systematic work was again instituted about seven weeks ago. The arm and hand movements are now nearly normal. There is no restriction of movement at the shoulder, nor is there any pain on complete circumduction at that joint. Gait is considerably better than it was, and the outlook for complete functional recovery is good.

CASE 3.—S. H., now aged 8 years, at the age of 6 had an acute attack of chorea, which became progressively worse. There were choreiform movements of all extremities. The face was continuously distorted by grimacing. Respirations were irregular, and speech was almost impossible. The child was moody, irritable, emotionally unstable, suspicious and difficult to approach. Later she became more cooperative and tried to help with the exercises. Though seen at irregular intervals, she began to improve, and after about ten weeks made a good recovery. The exercises should have been continued for some time after she recovered, but they were stopped by the mother. One year later the patient again began to have choreiform movements. Exercises were begun within two weeks after the onset of this attack; the child made a good recovery within eight weeks, and has been well since.

CASE 4.—H. B., a schoolboy, now aged 15½, at about the age of 4 began to show blinking of the eyelids. This soon extended to the muscles of the face, causing grimacing; at the age of 12, movements affecting the right shoulder and arm were added. With great effort the boy could suppress these movements occasionally for short periods. Neurologic examination revealed a typical clonic tic of the eyelids, moderately severe grimacing and a shrugging tic of the right shoulder and arm. Exercises were begun; within eight weeks the tic had disappeared. For the past three and a half years the patient has blinked the eyelids only when he became very excited and has been able to control this as soon as it was called to his attention.

DISCUSSION

DR. ISRAEL STRAUSS: Dr. Grossman has covered a phase of work neglected by neurologists. I do not refer particularly to the remarkable results which he has obtained in poliomyelitis, but to what he is able to do in ordinary cases of hemiplegia. Physical therapeutists can accomplish something in cases of poliomyelitis and hemiplegia, but they cannot do what an educated physician, especially a neurologist, can if he is willing to put the time and patience into the work.

DR. E. D. FRIEDMAN: I can verify the excellent results obtained in a severe case of poliomyelitis involving the lower portion of the cervical region of the cord. I believe that most neurologists pay little attention to the paretic limbs in cases of hemiplegia. Under the regimen which Dr. Grossman and some physical therapeutists carry out a good deal can be done for an apparently hopeless hemiplegia.

DR. RICHARD BRICKNER: Has it been possible to do anything in cases of paralysis agitans?

DR. MORRIS GROSSMAN: Unfortunately, no. I have tried in a number of cases.

CONGENITAL MULTIPLE INTRACEREBRAL AND EXTRACEREBRAL ARTERIOVENOUS COMMUNICATIONS WITH PSYCHIC CHANGES. DR. GEORGE V. N. DEARBORN.

A well developed white man, aged 43, a Jew, completed two years of evening high school at the age of 13. His disposition and habits were good. He married at 21; there were three children and no miscarriages. Because of fatigability and peculiar "spells," he worked half-time. He was discharged from the United States Navy in midsummer, 1918, because of "spells" of amnesia and aphasia, with pain in the left arm and beneath it. He did not fall in the attacks.

Examination of the occipital region disclosed pulsations and bruits on both sides; they were most marked over the left mastoid process and the occipital

arteries, but also present over the veins of the eyelids. Edema about the left orbit, arterial pulsation of the right eyeball and hemianopia were also present.

Dr. Walter E. Dandy, of Baltimore, reported: "Roentgen examination shows a remarkable picture; three kinds of changes are evident. In the occipital region, on the left side particularly, in the usual area of lesser density just above the site of the inion, the bone is grooved by little channels which seem to be of arterial origin. The arteries probably communicate with the venous system in the diploe. There is a huge channel in the left side running from the occipital to the temporal region; it is lost in the base of the skull, probably in the cavernous sinus. This channel becomes larger posteriorly; there are radiating channels that converge on it. There is also a group of veins, with one especially conspicuous, in the supra-orbital region. The third change is a great cluster of calcifications, occupying an area about as large as a hen's egg, in the left temporoparieto-occipital region. In two places there are thin parallel shadows, which probably represent vessel walls; there are several more diffuse shadows which seem to radiate to a central zone and seem to go below the surface into the depth of the brain for a distance of 2 or 3 cm."

It is obvious that a widespread and serious congenital arteriovenous angioma is present, being probably more marked in the left hemisphere; it has brought about fairly well defined, progressive behavior disturbances as well as unusual stereotyped attacks. The aneurysmal formations affect the occipital and left parieto-frontal regions; perhaps there is bilateral involvement of unknown extent.

DISCUSSION

DR. JAMES H. HUDDLESON: I saw this patient for a period of one month in 1922; the deterioration to which attention has been called was then not marked. The patient did not have the stereotyped attacks, so far as I recall. The signs were so few that a diagnosis of psychoneurosis was made. The patient's failure of cooperation and stubbornness were marked, even more so than Dr. Dearborn has described. Treatment was so ineffective on the basis of a probable psychoneurosis that within a few weeks he was returned for further examination, which shows that even at that time there seemed to be something that had not been detected in addition to a simple maladjustment. While this man had a serious disability, the maladjustment which he showed was typical of a compensation neurosis.

DISSEMINATED DISEASE OF THE NERVOUS SYSTEM OF UNKNOWN ETIOLOGY. DR. J. E. RUBINSTEIN (by invitation).

H. F., aged 33, a wholesale fruit dealer, was admitted to Montefiore Hospital on Jan. 25, 1934, with the complaint of poor vision and of difficulty in walking. In spite of his large size, he has noticed that he was not so strong as his fellow workmen for a number of years; he also has experienced numbness of the soles for the last four or five years. Since the summer of 1931, he has experienced a steadily progressive weakness of the lower extremities; in 1932 he noticed a slight but progressive diminution of vision; by July 1932, he was unable to distinguish green, and vision was blurred at night. During the latter half of 1932 he suffered from insomnia and lost about 50 pounds (22.7 Kg.). At that time he also began to experience pain in the right buttock, which was made worse by walking; this symptom has persisted intermittently up to the present. There also developed paresthesias of the left fingers, which later extended up to the hand and forearm. A marked numbness was felt, especially in the ulnar distribution of the left hand. A few months later the right hand became similarly affected. At the end of 1932, speech became thick, memory was poor, and the patient felt somewhat drowsy. At the same time libido diminished. By January 1933, vision had become very poor. At that time an intracranial neoplasm was suspected. but an encephalogram was reported as showing a normal picture.

The patient resumed work and was apparently somewhat improved until August 1933, when he suffered from severe headaches affecting the right eye and

temple. He became so weak that his legs gave way under him. He was then hospitalized for six weeks. On discharge, in October 1933, the diagnosis made was encephalomyelitis. Since October 1933, he has become a little stronger and has been getting about with the aid of a cane. He says that his handwriting is shaky, and he fumbles a little when reaching for things. Two weeks before admission to the Montefiore Hospital the right half of the head, including the right side of the buccal mucosa and tongue, became numb. There are no vesical or rectal disturbances; libido is practically gone.

The past and family history are without significance, except that the mother has been suffering from pernicious anemia for the past five years and is receiving liver therapy.

The patient has acromegalia, is 6 feet and 1 inch (185.42 cm.) tall, and weighs 190 pounds (86.2 Kg.). The general physical condition is essentially normal; there is evidence of loss of weight, and the musculature is flabby. He can hardly walk without support.

The patient has a waddling gait, walks on a broad base and does not lift his feet off the ground. He bends his body in an attempt to balance himself. Genu recurvatum is evident. The patient has great difficulty in arising from the recumbent position. There is slight ataxia, of the posterior column variety, in the hands and feet and no signs of cerebellar involvement. General muscular weakness and atrophy are present and are especially noticeable in the muscles of the hand; there is bilateral partial foot drop, with apparent hypertrophy of the muscles of the calf. No fibrillations are observed. The deep reflexes in the lower extremities are absent, and the abdominal reflexes are diminished; no pathologic reflexes are demonstrable, though there is no plantar flexion. Sensation is diminished for pain and temperature in a glove and stocking distribution. Position sense is lost in the toes, and vibratory sensation is lost below the iliac crests. Touch is impaired in the feet and at the tips of the fingers. The fundi show bilateral primary atrophy of the optic nerve, the left more than the right. The visual fields are normal, except for color blindness for green. The pupils are dilated and show the Argyll Robertson reaction. Nystagmus is present in all directions. There is slight impairment of sensory and motor functions in the right fifth nerve. Speech is hesitant and has a nasal quality. The patient seems euphoric and facetious; his memory is somewhat poor. The ulnar and common peroneal nerves are markedly thickened, cordlike and nodular.

Complete analyses of the blood and urine gave negative results, except for the arsenic content of the urine (0.027 mg. per liter).

The serologic tests of the spinal fluid and manometric studies gave negative results. On many occasions the fluid has shown a 4 plus reaction to the Pandy test; and the total amount of protein has ranged from 139 to 266 mg. per hundred cubic centimeters, and there have been as many as 15 cells per cubic millimeter. Gastric analysis gave negative results; free hydrochloric acid was present. The basal metabolic rate on two occasions was —31 and —27.

Roentgenograms of the skull and spine showed essentially normal conditions except for a slight hypertrophic spondylitis.

Summary.—The case shows dissemination through the central and peripheral nervous system, affecting primarily the peripheral and cranial nerves and partly the posterior columns of the spinal cord. In addition, the laboratory findings in the spinal fluid are unusual.

The different diagnoses that have been suggested are: (1) multiple sclerosis; (2) encephalomyeloradiculitis; (3) muscular dystrophy and (4) toxic degenerative disease. In my opinion, the condition is most likely a toxic degenerative disease, the etiology of which is unknown. There is probably an interstitial hypertrophic neuritis of Dejerine and Sottas.

DISCUSSION

DR. C. BURNS CRAIG: What was the progress of the case in the first year?

DR. J. E. RUBINSTEIN: It was intermittent. The patient was able to work for the first half year after he left the first hospital. Then he was rehospitalized

in another place and felt weak; he says now that he feels a little stronger; the present status is stationary.

DR. ISRAEL STRAUSS: What symptoms does Dr. Rubinstein think the patient has that are referable to the posterior column?

DR. J. E. RUBINSTEIN: There is diminution in vibration sense of both legs and feet; position sense is lost in the toes. There is a question also concerning ataxia referable to the posterior column in the upper extremities. My associates and I thought that it was slight.

DR. H. A. RILEY: Was the urine examined for lead?

DR. J. E. RUBINSTEIN: Yes, it was negative in a seventy-two hour specimen.

DR. H. A. RILEY: Was any histologic examination made of any of the nerves by biopsy?

DR. J. F. RUBINSTEIN: No.

DR. H. A. RILEY: Were any of the predominantly sensory nerves enlarged?

DR. J. E. RUBINSTEIN: That has not been demonstrated.

DR. S. P. GOODHART: This man's condition may be due to involvement of the peripheral nerves; the gait, however, is that seen in cases of dystrophy, and even more suggestive is the feel of the muscles of the calf, which are pseudo-hypertrophic and have that peculiar feel characteristic of dystrophic muscle tissue. If this man has dystrophy, it will cast some light on the real pathologic process of progressive muscular dystrophy, as a disease perhaps having its origin in the central nervous system.

QUESTION FROM AUDIENCE: Has the patient ever visited in the tropics?

PATIENT: No, I have been in Washington, Maryland and Virginia, but no farther south.

DISEASE OF THE SPINAL CORD FOLLOWING TRAUMA. DR. WILLIAM BERMAN (by invitation).

The patient, a peddler aged 60, was well until about four months ago when he was struck by an automobile. He was unconscious for four days after the accident. He was told that he had bled from the mouth on arrival in Governeur Hospital. When he regained consciousness he had severe pains, of squeezing and burning nature, in both arms; the fingers of both hands felt numb, and there was weakness in all muscles of both upper extremities. The pains in the upper extremities have persisted until the present, and are often shooting in character. After two weeks at the hospital he became psychotic and was transferred to the psychopathic division of Bellevue Hospital. The diagnosis on his discharge from the former hospital was fracture of the skull, traumatic psychosis and traumatic cerebral hemorrhage.

On admission to Bellevue Hospital, the patient was disoriented, boisterous, maudlin and at times semiconscious; he wept and laughed intermittently and frequently shouted loudly. It was necessary to restrain him. Several spinal taps disclosed bloody spinal fluid. The pupils were equal and regular but reacted rather poorly to light. Extra-ocular movements were normal; there was no nystagmus. Facial innervation was normal. The tongue was protruded in the midline. The deep reflexes were active and equal. No pathologic reflexes were found. There was weakness of the extensor muscles of the wrists, but no definite wristdrop. Slight swelling of the dorsum of the right hand was noted. After two weeks the patient was discharged, the diagnosis being traumatic psychosis and traumatic delirium.

He was admitted to Montefiore Hospital on Dec. 29, 1933. Examination revealed normal cranial nerves; symmetrical paralysis of the muscles of the upper extremities, increasing in severity distally; a weak hand clasp, and bilateral wrist drop; extension and flexion could be carried out only incompletely and with great difficulty. The muscles of the arms and forearms were flabby and atrophic, but no

fibrillations were seen. There were a suggestion of atrophy in the interosseus muscles and some edema of the hands. The muscles of the lower extremities were normal. The deep reflexes in the upper extremities could not be elicited. The left ankle and knee jerks were slightly more active than the right. A positive Oppenheim sign was elicited on the left, but there was no Babinski toe sign. Both plantar responses appeared to be normal. The abdominal reflexes were present and equal. The patient had sensory disturbances which could not be sharply delineated. It was obvious, however, that there was definite diminution of pain and temperature sense bilaterally in the segments from the fifth cervical to the second thoracic. Touch sense was disturbed in a patchy manner in this area. The sense of position in the fingers was lost, and vibration sense in the upper extremities was retained only in a patchy manner and was much diminished.

Roentgenologic examination revealed no evidence of a fracture of the skull but showed advanced hypertrophic spondylitis in the cervical region and moderate hypertrophic spondylitis in the thoracic region of the spine. The blood pressure was 138 systolic and 88 diastolic. The fundi showed moderately advanced retinal arteriosclerosis.

Since admission to the hospital, the patient has shown slight but definite improvement. The triceps reflexes have returned, and the sensory disturbances are now limited to the distal portions of the upper extremities. Also, the patient states that the spontaneous pains which were so aggravating are now not so severe in the arms and forearms, and are limited almost exclusively to the hands. Sweating and electrical tests have revealed no significant abnormalities.

It is obvious that this patient has sustained a definite injury to the brain—a concussion of the brain—although one cannot be certain of a fracture of the skull. It is likewise difficult at this time to determine whether the blood in the spinal fluid was of cerebral or of spinal origin. It is probable that the persistence of the signs referable to the pyramidal tract on the left are indicative of cerebral injury. In addition, there has undoubtedly been a segmental spinal injury. The suggestion has been offered that perhaps there was a spinal dislocation which reduced itself immediately following trauma, with perhaps some accompanying meningeal injury. The absence of sensory dissociation and of sensory signs below the level of the lesion indicate that there is not any profound disturbance of the sensory pathways within the cord itself, thereby excluding a diagnosis of hematomyelia. It seems more likely that there has been some type of traumatic injury to the spinal roots, involving both sensory and motor fibers and perhaps also the entrance zone of the dorsal roots.

DISCUSSION

DR. H. A. RILEY: Has a manometric determination of the spinal fluid pressure been made?

DR. WILLIAM BERMAN: The pressure was normal.

DR. C. BURNS CRAIG: What was the immediate effect of the accident?

DR. WILLIAM BERMAN: I did not see this man until one and a half months after the injury. At Bellevue Hospital the physicians reported weakness of the upper extremities; he was seen there about two weeks after the injury.

DR. E. D. FRIEDMAN: Why does Dr. Berman exclude hematomyelia so definitely? At this stage there is nothing that militates against a diagnosis of hematomyelia. This patient has spinothalamic sensory disturbances, which are bilateral, and localized atrophy of the muscles. At the onset of hematomyelia there are signs indicating a level and phenomena from pressure on the long tracts, but after a time they recede and the only residua are signs referable to the central gray matter, namely, atrophies and sensory changes of spinothalamic type.

DR. WILLIAM BERMAN: There has been discussion as to whether this is a central or a peripheral type of lesion. The picture has been that of a spinal lesion without central involvement; we thought that if the cord itself was involved, it was probably in the entrance zone of the dorsal roots.

DR. BYRON STOOKEY: Was there bladder or rectal disturbance?

DR. WILLIAM BERMAN: No.

DR. BYRON STOOKEY: Did I understand Dr. Berman to say that a roentgenogram of the spine showed hypertrophic arthritis?

DR. WILIAM BERMAN: Yes.

DR. BYRON STOOKEY: I think that it is possible to explain the lesion on the basis of the hypertrophic arthritis, with involvement of the emergent nerve roots, but this would depend on how severe the arthritis appeared to be. It would be entirely possible for a minor injury to precipitate marked paralysis in the presence of hypertrophic arthritis. I should question the diagnosis of hematomyelia. May I suggest that an oblique stereoscopic roentgenogram be taken first from one side and then from the other, to visualize the foramina of exit?

DR. ISRAEL STRAUSS: Has the possibility of tearing of the dura been considered?

DR. WILLIAM BERMAN: Yes. It was thought that there might be a pachymeningitis.

DR. ISRAEL STRAUSS: Were symptoms of hypertrophic spondylitis present before the accident?

DR. WILLIAM BERMAN: As far as is known there were not.

DR. ISRAEL STRAUSS: I do not know why it is supposed that the patient had a definite lesion before the trauma. Did he have pain of a root character?

DR. WILLIAM BERMAN: Yes, in the upper extremities since the accident. Recently the pain has subsided. There are shifting "squeezing and burning" pains.

TUMOR HIGH IN THE CERVICAL REGION OF THE SPINAL CORD SIMULATING COMBINED SYSTEM DISEASE. DR. WILLIAM SCHICK (by invitation).

This case is one of those uncommon instances of compression of the upper portion of the cervical region of the cord which expresses itself as combined disease of the posterior and lateral columns. Despite its supposed rarity, I have seen this clinical picture in four cases in various stages of development. In some, the diagnosis was made later than in the case to be presented because of the absence of subarachnoid block. Dr. E. D. Friedman first called attention to this interesting syndrome in 1929; since then a few scattered cases have appeared in the literature.

J. F., a clothes presser, aged 54, admitted to the Montefiore Hospital on Dec. 8, 1933, four and a half years ago began to complain of numbness in the fingers of both hands. This gradually extended upward to involve the forearms, and in about six months the lower extremities also. Two and a half years ago, after a trivial fall down a few steps, he complained of a sense of tightness about the left side of the chest and noticed that the left upper and lower extremities were becoming weak and stiff. This condition increased gradually; after a period, weakness and stiffness involved the right extremities also. He had no difficulties with the sphincter, suffered no pain and had no limitation of motion in the cervical region of the spine.

Physical examination revealed generalized arteriosclerosis, moderate hypertension and other findings of no special significance. Neurologically, there were generalized spasticity, motor weakness, hyperreflexia and bilateral signs referable to the pyramidal tract, all being more marked on the left side. Walking was difficult because of the spasticity. There was some slight wasting of the supraspinatus and infraspinatus muscles on the left. Vibratory sense was markedly impaired below the iliac crests, and somewhat less so over the thoracic region of the spine. Position sense was defective in the fingers and toes, but was least involved in the right foot. Objects in both hands were recognized poorly or not at all. There was no involvement of superficial sensation or spinal tenderness.

Spinal puncture revealed complete subarachnoid block; the spinal fluid was clear and xanthochromic, showed 4 cells, a good deal of globulin and a total

amount of protein of 350 mg. per hundred cubic centimeters. Cisternal tap revealed a similar fluid, slightly colored, with the total amount of protein 76 mg. per hundred cubic centimeters. Iodized poppy-seed oil 40 per cent injected into the cisterna magna was arrested at the third cervical vertebra. All other laboratory data were normal.

Operation by Dr. Ira Cohen revealed a tumor, about the size of a small finger, extending from the first to the fifth cervical vertebra. It was situated on the left posterior aspect of the cord, beneath the arachnoid, and was well encapsulated. The cord was indented and pushed forward and to the right.

An interesting feature is the practically complete recovery which has taken place in the few weeks since operation.

DISCUSSION

DR. H. A. RILEY: Was the localization made by the injection of iodized oil.

DR. WILLIAM SCHICK: Exactly. There was only one other feature which might have suggested the probable localization, and that was the atrophy of the supraspinatus muscle.

DR. SAMUEL BROCK: Was there any diaphragmatic involvement?

DR. WILLIAM SCHICK: No. The man had absolutely no limitation of movement of the cervical region of the spine before the injection of iodized oil, though the tumor had been present for almost four and a half years. He had been to three other hospitals before any one suspected the correct diagnosis.

DR. SAMUEL BROCK: What was the nature of the neoplasm?

DR. WILLIAM SCHICK: Meningioma.

DR. BYRON STOOKEY: I do not see why the case should be called a case of combined system disease. Localized atrophy in the deltoid and in the supraspinatus and infraspinatus muscles were noted. As far as I know, atrophy of this nature does not occur in combined system disease; it provides a definite point of localization. In tumors high in the cervical region of the spinal cord sensory examination is extremely variable and most unreliable; there may be little in the way of sensory change. In a case in which a tumor of the spinal cord is supposed to be in the upper cervical region, I feel that a cisternal puncture is contraindicated. One does not know how high a tumor of the spinal cord may reach. At operation on a number of occasions I have seen tumors high in the ventral cervical region of the spinal cord push the cord backward, and I have commented on the danger of doing a cisternal puncture in such cases. I think that this case showed a rather classic picture of a tumor high in the spinal cord, and I fail to see why it is reported as an instance of combined system disease.

DR. WILLIAM SCHICK: I agree with Dr. Stookey, with certain reservations. I do not think that this is a typical picture of extramedullary compression of the cord. The atrophy of the supraspinatus and infraspinatus muscles was a point in dispute and was by no means apparent to every one who examined the patient. In addition, a number of excellent clinicians examined the patient and did not suspect the presence of extramedullary compression of the cord. I have seen a number of similar cases in which for many months and even years a diagnosis of extramedullary compression was completely overlooked until iodized oil was injected.

DR. E. D. FRIEDMAN: These patients have presented essentially signs referable to the pyramidal tract and posterior column. The members of the neurologic staffs of Bellevue and Montefiore hospitals are good observers; some of us saw fibrillations and atrophies in the distribution of the upper cervical roots, but these were not conspicuous or consistent. One observer would see them, and another would not, and the patients for a long time were considered to have combined system disease. Later, with the advent of persistent fibrillation and advancing

muscular atrophy, the diagnosis became clearer. Some of these cases have for a long time been diagnosed as capsulothalamic disease. I think that it is important to call attention to this syndrome.

OTITIC HYDROCEPHALUS. DR. S. P. GOODHART and DR. NATHAN SAVITSKY.

G. M., a white man, aged 20, who was admitted to the Morrisania Hospital on Aug. 27, 1933, for two weeks before admission had had pain in the left ear after swimming. Four days later pus flowed from the left ear. After this apparently spontaneous perforation of the left ear drum the pain became less. Five days before admission he noted severe frontal headaches. He vomited ingested food a number of times before entrance to the hospital. He began to perspire excessively a few days before and for five days there was fever, his temperature varying from 101 to 105 F.

On admission he appeared acutely ill and complained of a throbbing headache. The left ear was discharging pus; no tenderness over the mastoid or sagging of the wall of the canal was present. There was bilateral papilledema of 1 diopter, but no evidence of focal involvement of the nervous system except horizontal nystagmus to both sides, depressed tendon reflexes and absence of the left ankle jerk, which was probably a sequel of poliomyelitis seventeen years before admission. There were no meningeal signs.

Spinal tap showed increased pressure (38 mm. of mercury), an Ayala index over 10, 30 cells, increased protein and a few gram-positive extracellular organisms. These organisms were seen only on smear. Cultures were sterile. The cells in the spinal fluid were all lymphocytes. The content of sugar and chloride of the spinal fluid was within normal limits. The Queckenstedt test showed no block. There was striking and persistent relief of the headache following the removal of 30 cc. of spinal fluid. Lumbar punctures were done daily for therapeutic and further diagnostic studies.

The patient continued without objective signs and appeared to be comfortable and not as sick as one would expect from the fact that the temperature was of septic type from admission to the day of operation, September 6. On Sept. 5, 1933, sagging of the posterosuperior wall of the canal on the left side was noted, as well as definite tenderness over the mastoid. A simple mastoidectomy was done, and the lateral sinus was exposed to the knee. No evidence of sinus thrombosis was seen.

Spinal taps after admission and up to the time of operation showed mild pleocytosis, a normal sugar and chloride content and some increase in the protein. Gram-positive diplococci, resembling pneumococci, were seen on smear, though cultures never gave positive results. The same organism, though in much greater numbers, was found in the purulent discharge from the ear. Soon after the operation the spinal fluid became normal except for persistently increased spinal pressure. The papilledema and the increased pressure of the spinal fluid continued for over a month without any cells or organisms in the fluid.

The temperature came down to normal after the operation, and the papilledema regressed. There were no subjective complaints. There was slight elevation of both disks at the time of the patient's discharge on Oct. 10, 1933.

Comment.—There was no sinus thrombosis to account for the papilledema. There was no abscess of the brain. Even if there were a few mural thrombi without occlusion of the sinus, the problem of the pathogenesis of the papilledema would remain unsolved.

This case probably is an instance of the otitic hydrocephalus recently described by Symonds. It is a serous meningopathy or acute hydrocephalus resulting most likely from a sudden increase in the rate of production of cerebrospinal fluid. This disturbance in the circulation of the cerebrospinal fluid is related in some way to the existence of a purulent focus within the skull. Otologists and neurologists have expressed a great deal of doubt about the justification for the creation of this disease entity. The presence of a sympathetic meningitis at the onset does

not have any bearing on the problem of the presence of otitic hydrocephalus. Symonds has recorded similar meningeal complications.

We wish to reemphasize that the presence of organisms in the spinal fluid does not necessarily indicate the presence of a bacterial meningitis. One must have biologic evidence of the virulence and activity of such micro-organisms. Such bacteria in the spinal fluid may be of attenuated virulence or even entirely inactive. The clinical picture was hardly that of bacterial meningitis. Dr. Josephine Neal said that these organisms were probably devitalized or of attenuated virulence. Chemical studies of the spinal fluid showed no evidence of activity of micro-organisms.

A striking fact was the apparent comfort of the patient despite persistent increase in intracranial pressure and the striking relief after one lumbar puncture.

The Ayala index was over 10. This rachidian index may occasionally be of value in differentiating a focal lesion from a serous meningopathy or hydrocephalus. This index is the ratio of the product of the final pressure and the amount of spinal fluid removed to the initial pressure. With increased pressure of the spinal fluid, an index below 5 is presumptive evidence of the existence of a focal lesion, such as an abscess. We recently studied a case of proved abscess of the temporosphenoid lobe with minimal focal signs in which the index was below 5. The value of this procedure merits further investigation.

DISCUSSION

DR. SAMUEL BROCK: The cases that Symonds collected were absolutely abacterial, and usually showed no pleocytosis. Symonds stated: "The cerebrospinal fluid in the fully developed state is under increased pressure, but clear and contains no excess of cells or protein. In those cases in which there is a preliminary phase of meningitis, the cerebrospinal fluid examined at this stage shows an excess of cells and protein." What do the presenters mean by "reaction"?

DR. S. P. GOODHART: The presence of pleocytosis.

DR. SAMUEL BROCK: And of organisms?

DR. S. P. GOODHART: No. If one accepts the report that organisms were found, certainly during the time of their presence the term otitic hydrocephalus would not be justified.

DR. ISRAEL STRAUSS: Were pneumococci found on two occasions?

DR. S. P. GOODHART: They were reported on more than two occasions, but I understand that Dr. Neal, to whom the slides were submitted, did not believe that they were septic organisms; her opinion was that if they were pneumococci they certainly were attenuated organisms since they could not be cultured.

DR. ISRAEL STRAUSS: What type of pneumococcus?

DR. S. P. GOODHART: It was said to have been type IV.

DR. ISRAEL STRAUSS: Was a blood culture made?

DR. NATHAN SAVITSKY: A number of blood cultures were made; all were sterile.

For a number of weeks the patient had papilledema and increased spinal fluid pressure with normal spinal fluid, no cells and no bacteria; so there must be some factor to account for the hydrocephalus other than the organisms that were found. I think that we are justified in calling this case one of otitic hydrocephalus.

ABSCESS OF THE BRAIN FOLLOWING ENUCLEATION OF THE EYE FOR A MALIGNANT GROWTH. DR. S. P. GOODHART and DR. NATHAN SAVITSKY.

C. V., a Venezuelan woman, aged 48, was admitted to the Morrisania Hospital on Dec. 2, 1932, in a semistuporous condition and unable to talk. Her father died from some type of mental disease. She had always been well up to the onset of the present illness. Two and a half years before admission she had noticed

a small mass on the right eyelid which grew in size. Six months later this small tumor was operated on and found to be a malignant epithelioma. She was well for eight months. She then began to feel severe and piercing pains in the right eye. Radium was applied over the eye for eight days. This resulted in an extensive dermatitis. The pain in the eye continued. The patient then came to the United States from Venezuela. The eye was enucleated at the Memorial Hospital on June 1, 1932, and eight days later radium needles were applied to the socket. The pain persisted. The spinal fluid on Sept. 1, 1932, was normal. The patient felt better and was fairly comfortable during October 1932. After tonsillitis in the middle of November, she began to feel weaker and became semistuporous. At times she seemed confused and rambled in talking. Convulsive seizures in the left upper extremity appeared, though details of this onset and frequency are not available. She had not spoken for six days before admission.

When admitted to the hospital she appeared acutely ill; her temperature was 100.8 F.; the pulse rate was 120, and the respiratory rate, 24. She was semicomatose and did not talk. There were purulent material in the socket of the right orbit and evidence of destruction of the roof of the orbit. There were râles at the base of both lungs, bedsores on both buttocks and an injected throat. The patient was incontinent. The neck was slightly rigid, with a bilateral Kernig sign. The left upper extremity was weak and showed some spasticity. The left abdominal reflexes were not obtained; there was no Babinski toe sign and no confirmatory signs. The grasp reflex was not tested. The left pupil reacted to light and in accommodation. The left fundus was normal. There was facial weakness on the lower left side; the patient responded to painful stimuli. She made no contact with the environment and remained mute to the end. There was no particular affective display.

The spinal fluid was normal and under a pressure of 9 mm. of mercury. The urine was normal. Studies of the blood chemistry gave normal results. The blood count showed 11,300 white cells, with 68 per cent polymorphonuclear and 32 per cent mononuclear cells.

Three days after admission the patient had a general convulsion, which was more marked on the left side. The nuchal rigidity increased; the coma deepened, and the patient died four days after admission to the hospital.

Autopsy showed absence of the right eye and an orbit filled with purulent material. On the orbital surface of the right frontal lobe was an abscess cavity, ¾ inch (1.9 cm.) in diameter, filled with purulent material. The orbital process of the frontal bone, just adjacent to the abscess, was the seat of a necrotic process, so that the anterior fossa communicated directly with the right orbit. There was some purulent fluid in the subarachnoid spaces. A smear showed organisms in the subarachnoid spaces, which proved to be Pneumococcus type IV. The internal auditory apparatus and sinuses were normal.

Microscopic diagnosis showed parenchymatous degeneration of the liver and kidney and congestion of the spleen, abscess of the brain in the right frontal lobe and meningitis.

AN UNUSUAL COMPLICATION IN THE NERVOUS SYSTEM FOLLOWING SPINAL ANESTHESIA. DR. S. P. GOODHART and DR. NATHAN SAVITSKY.

T. H., a white woman, aged 32, was admitted to the Morrisania Hospital on Sept. 23, 1934, suffering from an anal fistula. For a short period before admission she had complained of pain in the rectum and bloody stools. For eleven years she had had varied complaints referable to the gastro-intestinal tract: nausea, vomiting, abdominal pain and occasional hematemesis. A series of studies of the gastro-intestinal tract was made in September 1930, but no organic lesion was found. Gastric analysis showed no free hydrochloric acid or lactic acid. After discharge from the hospital in 1930 the patient was sick for about two months with icterus and pain in the right hypochondrium.

Of particular interest was an incident which occurred fourteen years before admission to the hospital. A local anesthetic was injected by a dentist into the upper gums on the right side in the course of dental treatment. A few hours afterward the right cheek became swollen, and within six hours the right eye was closed by the swelling; the tissues of the right side of the neck also were involved; the palate became swollen, and the patient was unable to open her mouth. She had to be fed by tube. She was drowsy and restless at the time, but was relieved somewhat by an incision of the palate. She remained in bed for two weeks and recovered; physicians and dentists told her that she is sensitive to "cocaine." She never permitted the use of a dental local anesthetic again.

Physical examination on admission showed some tenderness in the left hypochrondrium and right lower quadrant of the abdomen, but no rigidity and no masses were felt. There was no evidence of focal disease of the nervous system. Hemorrhoids and an anal fissure were present.

On Oct. 10, 1932, she was given 12 mg. of procaine hydrochloride intrathecally and was operated on for the hemorrhoids and anal fissure. The postoperative course was uneventful until the fourth day, when she complained of difficulty in speaking and swallowing. Neurologic examination on October 18, four days after the onset of these symptoms, showed: right-sided peripheral facial paralysis; complete nerve deafness on the right side; motor and sensory involvement of the fifth nerve on the right side; right palatoplegia; diminution of the gag reflex on the right; great difficulty in protruding the tongue; weakness of both sternocleidomastoid muscles and the right trapezius muscle; left-sided deep hyperreflexia; weakness and adiadokokinesis of the upper limb, more on the right; bilateral finger-to-nose ataxia; no nystagmus; segmental diminution of sensation, superficial modalities from the fourth cervical to the first thoracic segment on the right, and in the second and third sacral segments bilaterally; absence of vibration in the left upper limb and over the left hip; much diminished abdominal reflexes on the left side; a positive Hoffmann sign on the right; no Babinski sign or confirmatory signs.

On the next day there was marked improvement; the nerve deafness was less marked, the facial paralysis was much improved, and the segmental sensory changes were less evident. Improvement was progressive and rapid, so that on October 24, ten days after the onset of this complication, neurologic examination gave entirely negative results. There was some headache throughout the ten days. There were no meningeal signs.

Laboratory studies gave negative results. A spinal tap on October 20 yielded clear fluid with 6 lymphocytes, no increase in globulin, and sugar. Laryngoscopic and ophthalmoscopic examinations gave negative results.

Allergic skin tests with procaine gave negative results.

Summary.—There was transitory involvement of the central and peripheral nervous system following the spinal anesthesia: toxic neuritides of some of the cranial nerves on the right side (fifth, seventh, eighth, ninth, tenth [?], eleventh and twelfth), involvement of the pyramidal tract and cerebellar pathway and implication of many of the spinal nerve roots.

Comment.—While Kay, Devraigne and his associates and others have recorded instances of extensive involvement of the nervous system following spinal anesthesia, we have not been able to find any case with a complication similar to that observed in this case. The benign course of the complication is noteworthy and in contrast to the apparent severity of the clinical picture soon after the onset. The sixth nerve, most frequently affected after spinal anesthesia, was spared.

The history of a severe reaction to a local anesthetic fourteen years before suggested the possibility of the existence of an unusual sensitivity to local anesthetics in this case. The patient was warned not to permit the use of local anesthetics. The history of such a reaction should make one unusually careful about giving spinal anesthesia. The purpose, however, of this communication is to put on record an unusual complication of spinal anesthesia.

DISCUSSION

DR. ISRAEL STRAUSS: When the dentist injected procaine hydrochloride, did the face become swollen at once?

PATIENT: No, seven hours later.

DR. ISRAEL STRAUSS: Was the cheek also swollen?

PATIENT: Yes, and a red spot showed on it; then the throat itself became swollen.

DR. ISRAEL STRAUSS: That was within a few hours?

PATIENT: From seven to eight.

DR. ISRAEL STRAUSS: After the injection, was any pain felt in the face?

PATIENT: Yes, a severe pain.

DR. ISRAEL STRAUSS: I am questioning the sensitivity to cocaine. What drug was used for the spinal anesthesia?

DR. S. P. GOODHART: Procaine hydrochloride, 12 mg.

DR. ISRAEL STRAUSS: I wish to comment on the idea that the first injection of the drug indicated a sensitivity to the subsequent use of a related drug. I do not believe that this manifestation had anything to do with the sensitiveness to this drug. I believe that what happened was that the dentist probably infiltrated the tissues and may have caused hemorrhage and tissue reaction, because within a few hours the face was swollen, and there were swelling inside the mouth and extreme pain. Recently I saw the same condition following local anesthesia for extraction of a tooth. There was an extravasation of blood underneath the skin, which indicated a deep hemorrhage.

DR. S. P. GOODHART: I do not know of any way in which one could determine whether the first dental complication was due to infiltration or to sensitivity. We did not see the patient at the time. We do know that there was extensive local anesthesia. We merely mention the possible relationship between what appears to have been sensitivity to cocaine and the unusual results following spinal anesthesia.

LESION OF THE POSTERIOR FOSSA WITH ATROPHY OF THE OPTIC NERVE AND WASTING OF THE LEFT TRAPEZIUS MUSCLE. DR. SAMUEL C. BURCHELL.

This patient has had headaches and attacks of dizziness for six months. He presents a mild cerebellar disturbance of gait, atrophy of both optic nerves and contraction of the visual fields. There is a marked and progressive atrophy of the left sternocleidomastoid and trapezius muscles. On two occasions a block has been demonstrated by manometer. On two occasions an encephalogram has shown that no air entered the ventricles, but a large collection of air was present in the basal cistern, more on the right than on the left. The case is presented for diagnosis. A left posterior fossa neoplasm extending to or through the foramen magnum has been considered the most probable diagnosis.

DISCUSSION

DR. GEORGE H. HYSLOP: Some years ago I saw a man, aged about 20, with congenital syphilis who, after trauma in the upper part of the cervical region, had internal hydrocephalus, papilledema, rigidity of the neck, impairment of the anterior horn cells in the upper part of the cervical region and defective sensation of the pathways of the spinothalamic tract; he had a spinal block. The level of signs was in the upper part of the cervical region of the cord. Operation showed a dilated central canal. Whether or not the congenital syphilis had any causal relationship was not determined. In the patient presented by Dr. Burchell, I think that there may be a dilatation of the central canal in the upper part of the cervical region.

NEUROPSYCHIATRIC SYMPTOMATOLOGY IN A CASE OF HYPOGLYCEMIA. DR. LAURENT FEINIER.

A woman, aged 33, was admitted to the Fourth Division of the Neurological Institute on Aug. 26, 1933, and discharged on Jan. 6, 1934. On entry she was in a comatose state, having lapsed into unconsciousness two days before. Six months ago she began to complain of headaches, which were generalized and pressure-like; they later tended to become more frontal. The patient had been considered nervous; manifestations of irritability and depression were usually more prominent at the menstrual periods, when the headaches were worse and accompanied by dizziness. On one occasion, following a period of depression and agitation, she attempted to commit suicide by jumping from a window, but was restrained; following this episode she was resistive and agitated. During this period peculiar movements of the body were noted; she would become somewhat rigid and tremulous, which was followed by periods in which she would kick and shout and show increased salivation and some drooling. Other attacks occurred in the four months preceding admission; the patient became disturbed, and would sneer, giggle and grimace. No definite convulsive movements were noted. Two months before admission the patient had a vomiting spell, which was nonprojectile; not long after this she suddenly collapsed and exhibited a staring expression, with wandering movements of the eyes, some shaking movement of the body and grimaces. The seizure lasted for two hours. She was not able to recall what had happened during the attack. Two days before admission she complained of headache and dizziness, following which there were grimaces, giggling, inability to respond to questions and trembling movements of the body. On the following day she vomited and was unable to talk. She appeared pale. Two family physicians reported that they had found the patient to be suffering from a nervous breakdown. These opinions are inserted merely to emphasize the initial impression one is likely to receive in these cases.

On admission to the hospital the patient was in coma, with pupils widely dilated and scarcely reacting to light. The left side of the face was somewhat flattened. The abdominal reflexes were absent; the knee jerks were unequal, the right being greater; the ankle jerks were difficult to elicit. There was slight rigidity of the neck. Definite hypertonus of the upper extremities and a bilateral Babinski sign were found. The disks appeared normal, with moderate distention of the veins. There was excess salivation, with drooling from the mouth. No particular attitude was noticed. Respirations varied in depth as well as in duration, but were not of any special type. There were periods of rolling, wandering movements of the eyes, which were momentary and associated with grimacing. The blood pressure was 120 systolic and 80 diastolic. The temperature varied from 101 on admission to 105.4 F.; in the second week, from 98.2 to 103 F. The pulse rate varied from 100 to 135. The condition was tentatively considered to be encephalitis of unknown etiology; forced drainage, with 500 cc. of 25 per cent dextrose solution intravenously, was carried out. The blood chemistry on Aug. 28, 1933, showed a sugar value of 154 mg. per hundred cubic centimeters. Dr. Soltz noted that the next sugar determination, made some time later, showed a value of 65 mg. Subsequent daily estimations of blood sugar for five days ranged between 38.5 and 57.7 mg. The patient then fasted for thirty-six hours. The blood sugar showed a progressive fall from 7:35 a. m., when the value was 52.6 mg., to a minimal value of 37.5 mg. at 11:10 a. m., following which the amount progressively rose, without any food having been administered, to a maximal value of 63.8 mg. The patient was considered to be suffering from hypoglycemia. A sugar tolerance test on November 9 revealed: during fasting, at 10:10 a. m., 30.3 mg.; during fasting at 10:30 a. m., 34; at 11:20 a. m., 101.3; at 11:50 a. m., 112.7; at 12:15 p. m., 147; and at 12:45 p. m., 163.

A description of the attacks follows: The patient grew restless and apprehensive and complained of nervousness and dizziness; breathing became stertorous. She perspired profusely, did not speak, became rigid, expectorated into her hand and threw the sputum about, was difficult to keep in bed and was incontinent. In

other attacks she grimaced, snorted, tossed about, twisted her hands, laughed, screamed and shouted. The hands were cold and clammy.

Extract of suprarenal cortex, whole dried pituitary substance, whole dried suprarenal substance, epinephrine, pituitary and insulin were administered. None of them produced any significant change in the blood sugar levels. When the patient was given dextrose intravenously, and later a diet high in carbohydrates, the attacks were reduced to about one in three weeks.

On Jan. 11, 1934, the patient was operated on by Dr. Whipple at the Presbyterian Hospital; an adenoma of the pancreas was removed, following which the neuropsychiatric symptoms ceased and the blood sugar returned to normal.

All cases of hypoglycemia and even of hyperinsulinism are not caused by neoplasms, but even when other etiologic factors cannot be demonstrated removal of part of the pancreas may have beneficial results by reducing the amount of overactivity of the islet cells. It appears that studies of the blood sugar should always be made in the case of a patient suffering from mental symptoms with involuntary movements and disturbances of consciousness.

DISCUSSION

DR. BELA MITTELMAN: Did the patient ever complain of hunger or thirst?

DR. LAURENT FEINIER: Hunger and thirst were not marked; dizziness and headaches were the subjective symptoms. She did not stress hunger or that "all-gone" feeling. On one occasion she did say, "Save me!" and had a feeling that she was going into an attack.

DR. JOSEPH SMITH: Was she ever confused?

DR. LAURENT FEINIER: Between attacks she would be clear and cooperative.

DR. JOSEPH SMITH: Was she very sick? Did she appear hysterical?

DR. LAURENT FEINIER: No, between attacks I did not think she appeared very sick, nor did she appear hysterical. In the episodes she appeared more psychotic than hysterical; on one occasion a spinal needle was broken.

DR. C. BURNS CRAIG: Were there any hemorrhages into the tumor?

DR. LAURENT FEINIER: None were reported; the growth was regarded as a typical adenoma of the islet cells.

DR. GEORGE H. HYSLOP: What had Dr. Feinier to say with respect to persons who have a functional hypoglycemia, with an associated vascular hypotension, an asthenic habitus and the behavior and personality changes which so often on superficial examination lead to a diagnosis of an anxiety state. Actually, in such cases the personality disorder is a sequel to a physiologic defect, which may be the result of overexertion, focal infection or other somatic stress, and is decidedly not the effect of a psychic maladjustment.

DR. LAURENT FEINIER: I am sorry I cannot adequately answer Dr. Hyslop. I suspect that there is a large field in that direction. I am reviewing the blood chemistry slips of the Neurologic Institute in order to pick up some unrecognized low blood sugars, but as yet I have not come to any conclusion.

DR. BELA MITTELMAN: Hypoglycemia is a symptom. This patient's condition should be called hyperinsulinism. Hypoglycemia occurs in many different conditions, such as Addison's disease, pituitary states, poisoning, etc., but when there is a definite adenoma of the pancreas, as here, the condition should be called hyperinsulinism. One of the most characteristic features of hyperinsulinism is that it is intermittent; most of the time the blood sugar is normal, but there are attacks of hypoglycemia. Such an attack occurs when insulin is thrown into the blood stream by the pancreas (adenoma), and the patient's symptoms then make their appearance. What were this patient's symptoms with various levels of blood sugar? Patients react differently to various blood sugar values. Some patients may show signs of mental disturbance when the blood sugar reaches

55 mg. per hundred cubic centimeters. Did the patient ever show high blood sugar values? Some patients may show an alternation of high with low values.

DR. LAURENT FEINIER: This patient never showed high blood sugar reactions that I am aware of. I entirely agree that this condition could more specifically be called hyperinsulinism rather than hypoglycemia. I chose to call it hypoglycemia because I think the subject covers a much larger field than is generally recognized, and this would help to call attention to it. The patient usually was at her worst when the blood sugar was lowest, but this was not uniformly so.

DR. CHARLES ROSENHECK: Was there a periodicity in the recurrence of the attacks? What is the explanation for the presence of the Babinski phenomenon during and since the cessation of the psychotic behavior?

DR. LAURENT FEINIER: The attacks were irregular. At first the patient had a severe one, which lasted five days with a severe rise in temperature. Then, on a diet high in carbohydrate, the attacks were reduced to one in three or four weeks, in a fairly regular sequence.

As to the mechanism of the neurologic changes, I do not know whether insulin has a vagotonic or angiospastic effect on the vessels, with consequent starvation of the nerve cells, or whether the lack of dextrose and lactic acid serves to furnish a basis for nerve starvation and alteration of function; it is difficult to say on the basis of a single case. I think that there is some evidence of involvement of the central nervous system in this case, as shown in the slight residual signs of focal character. In dogs, following excessive injections of insulin, Bowers and Beck described pathologic changes, including edema, hyperemia and hemorrhages.

DR. S. BERNARD WORTIS: I wish to add a word about the relationship of the clinical findings in such cases of hyperinsulinism to the present knowledge of the metabolism of the brain. Both lactic acid and dextrose are absorbed by the brain from the blood in normal, phlorhizinized and depancreatized dogs. The brain does not convert or store these foodstuffs as glycogen. The cerebral utilization of both dextrose and lactic acid (each of which in oxidizing yields a respiratory quotient of unity) represents a factor of safety in the metabolism of the central nerve tissue. Insulin diminishes the consumption of oxygen of the cerebral cortex and likely results in anoxemia of the tissue (Wortis, S. B.: *Am. J. Psychiat.* **13**:729 [Jan.] 1934).

The blood dextrose (the chief brain fuel) and the content of lactic acid in the brain seem to be directly related; i. e., the lower the blood sugar, the lower the level of lactic acid in the brain. Convulsions and increased activity of patients with hypoglycemia as a result of hyperinsulinism may be evidence of a physiologic attempt to acquire homeostasis by increasing the lactic acid content (also a brain fuel) of the blood. Normally, there is from 10 to 15 mg. per hundred cubic centimeters of lactic acid in the blood; after a convulsion this may rise to as high as from 200 to 250 mg.

DR. CLARENCE P. OBERNDORF: It seemed to me that the picture described was one of a toxic disorder, probably due to starvation, such as one sees in exhaustion and infection when a person becomes confused, somewhat anxious and perhaps disoriented and stays in such a state for some time. I should say that a case of this type with so obscure a cause for the exhaustion might easily be mistaken, unless a careful examination such as was made, for one of anxiety hysteria. The case was probably so considered by the physicians who first saw the patient, emphasizing again the necessity for physicians who approach things from a purely functional angle to be on the lookout for such unusual phenomena.

DR. RICHARD BRICKNER: I am not certain that the particular attack which caused this patient's admission to the hospital was not encephalitis, in addition, of course, to the hypoglycemic state. The attack was different from any other which she had had before or has had since; it included a rise of temperature to 105 F., and a mild pleocytosis of the spinal fluid—phenomena not generally associated with hypoglycemia, as far as I know. This possibility has no relationship,

of course, to the hypoglycemic phase of the condition, yet I think it worth keeping in mind because of the chance of future complications.

DR. LAURENT FEINIER: Does Dr. Brickner mean toxic encephalitis?

DR. RICHARD BRICKNER: No, epidemic encephalitis.

DR. LAURENT FEINIER: I think that hypoglycemia covers the entire clinical situation. There was nothing abnormal in the blood count; the spinal fluid showed 15 cells and 42 mg. of protein. There were repeated periodic attacks of the same general nature, even though they were less severe.

While the literature mentions a few cases, we did not find many thoroughly described from the neuropsychiatric standpoint. Among twenty-nine cases reviewed by Gammon and Tenery, there were twenty-four in which there was some mental or nervous disturbance, incompletely described, nineteen in which there were convulsive disorders.

AURICULOTEMPORAL SYNDROME. DR. WILLIAM NEEDLES.

The patient, a white man, aged 34, a machinist, entered the neurological clinic of Mount Sinai Hospital in December 1933, complaining that whenever he ate profuse perspiration appeared over the right side of the face. At the age of 10, he had noticed a swelling in front of the right ear. When he was about 20, a surgeon operated on this mass, removing some soft tumor tissue. Following the operation, paralysis of the right side of the face ensued. Also, shortly after the operation, a fistulous opening appeared at the site of operation from which whenever the patient ate some fluid exuded. About six months after the first operation, a physician applied some substance, presumably a caustic, to the fistulous opening and sealed it. Now, whenever the patient eats marked sweating occurs over the right cheek. The reaction is most pronounced with spicy foods.

General medical examination gave negative results. Neurologic examination disclosed paresis of the right side of the face, with associated movements at the corner of the mouth whenever the patient blinked, reflexly or voluntarily. Taste was intact. There was diminution of pain, temperature and touch sensibility over the distribution of the right auriculotemporal nerve. When the patient was given an apple to eat, there appeared redness and then perspiration in the zone supplied by the auriculotemporal nerve. When, subsequently, the anterior two thirds of the tongue on the right side was swabbed with lemon juice there was no reaction; when the posterior third was swabbed, perspiration appeared promptly. When pilocarpine was administered hypodermically, sweating appeared more profusely over the right side of the face. On the other hand, atropine produced a diminution in the sweating reaction when taken before the patient ate. Stenson's duct was found to be patent and functioning normally.

A number of theories have been suggested in explanation of the auriculotemporal syndrome. In the present case it seems that the phenomenon is due to pressure on the vegetative nerve fibers, which accompany the auriculotemporal nerve, by the parotid gland as it swells during the act of eating. This explanation is confirmed by the fact that the disturbance made its appearance only after the escape of saliva, via the fistulous opening, had been hindered. Similar cases have been recounted in the literature on the subject.

This patient is to receive radiotherapy to the right parotid gland in an endeavor to render the gland functionless.

INTRACRANIAL ANEURYSM. DR. NATHAN SAVITSKY.

H. B., a man, aged 53, was admitted to Mount Sinai Hospital on Sept. 28, 1933, complaining of severe pain over the left side of the head and diplopia for eight days. For two weeks before the onset of these symptoms he had noted headaches and dizziness, which had been increasing in severity. His glasses were changed, with no improvement. About ten days before admission, on arising one morning he suddenly became dizzy and fell backward; yet he felt well enough that morning to go to work.

The pain on the left side of the head appeared suddenly and rapidly increased in severity. It was a dull ache with frequent paroxysms of sharp pain which were not relieved even by morphine. The diplopia appeared simultaneously with the left frontal pain.

Examination one day before admission showed: edema of the left upper lid; incomplete ptosis on the left side; a dilated left pupil, fixed to light and on accommodation; absence of the right to left consensual reflex; left external strabismus; weakness of all muscles supplied by the third nerve and questionable involvement of the superior oblique muscle; marked hyperalgesia in the first two divisions of the left fifth nerve, much more marked in the first division, and some retinal arteriosclerosis. Compression of the vessels of the neck on the left side resulted in the striking disappearance of the pain in the region of the left side of the forehead; it returned immediately on releasing this pressure. The blood pressure was 130 systolic and 80 diastolic.

On admission to the hospital the pain seemed to be less marked, and the edema of the left upper lid was no longer present. Neurologic examination showed paralyses of the third and fourth nerve on the left side and hyperalgesia in the first division of the fifth nerve on that side. Some fibrillary twitchings were noted in the muscles on the left side of the chin. The patient had had Bell's palsy on the left side three years before admission. No residual signs of this condition were found.

The spinal fluid was clear, with no evidence of recent leakage of blood into the subarachnoid spaces. Manometric studies gave negative results.

The patient left the hospital on October 15, much improved. The pain on the left side was much less severe, though diplopia persisted. For a short period after discharge, the left corneal reflex was diminished. At the same time a mild infection of the left conjunctiva developed; this cleared up rapidly under local treatment. The palsy of the oculomotor and trochlear nerves gradually disappeared, so that by December 14 no traces of any weakness of the ocular muscles were found. The man is now working. He still complains of occasional pain in the left side of the forehead. The hyperalgesia in the first division of the fifth nerve is still present. There is no weakness of the ocular muscles.

This is an interesting problem for diagnosis. There was sudden onset of a sphenoid fissure syndrome in a man with arteriosclerosis. There was never any fever. The pain was strikingly relieved by compression of the vessels of the neck. I believe that this is a case of an unruptured aneurysm in the region of the sphenoid fissure, probably arising from the circle of Willis. Fuller Albright described similar cases after rupture and with autopsies. An aneurysm in the region of the sphenoid fissure may suddenly grow larger without rupture, and give rise to a clinical picture such as this patient showed. I have seen a number of cases identical with this, except that in addition there was evidence of spontaneous subarachnoid hemorrhage. Many cases now called ophthalmoplegic migraine, neuralgia of the supra-orbital nerve and palsy of the third nerve of unknown etiology may well be unruptured aneurysms of the circle of Willis.

DISCUSSION

DR. SAMUEL BROCK: Have there been any roentgenographic studies?

DR. NATHAN SAVITSKY: Yes.

DR. SAMUEL BROCK: At the New York Neurological Institute, Dr. C. G. Dyke has demonstrated in a number of instances a characteristic crescentic shadow, which makes the diagnosis even more definite than does the temporary relief by compression of the vessels of the neck.

DR. RICHARD BRICKNER: While I think it is justifiable to believe that ophthalmoplegic migraine is of organic origin, an aneurysm was found in only one of the seven autopsies on record. Most of the cases start in childhood and last a long time. The usual finding at autopsy has been a fibroma or a tuberculous lesion.

PHILADELPHIA PSYCHIATRIC SOCIETY

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JOSEPH YASKIN, M.D., *President, in the Chair*

COEXISTENCE OF PSYCHOSES OF A DIFFERENT NATURE AND THEIR RELATION TO THE PERSONALITY OF THE PATIENT. DR. ALFRED GORDON.

Association of psychoses or succession of different forms of psychotic disturbances in the same person are not frequent; nevertheless, they are occasionally encountered. Recognition of the possibility of such a complication and analytic appraisal of the various manifestations will lead, I believe, to the view that the coexistence is not a mere coincidence, but that there is a significant interrelationship of the various phenomena. An example is presented here with reference to dementia paralytica.

The occurrence of catatonic manifestations in the course of dementia paralytica has been observed by a few authors. Examples can be found in the works of Knecht and Nacke. Careful reading of the life histories in the cases described will reveal that a large number of the patients presented inveterate constitutional tendencies characteristic of the schizoid type and that some of them presented phenomena characteristic of dementia praecox at different periods of life before the onset of the incidental dementia paralytica. These cases, as well as the one to be described, are not examples of a mere coincidence of two psychoses in the same person, but appear to be in close relationship with one another: The pathologic lesions of one served as a point of departure for the full development of the other, and the latter possessed a background subject by its very nature to easy psychologic dissociations and therefore to a splitting of personality, so characteristic of schizophrenia as an affective disease process.

The patient presented a striking transformation of a typical picture of dementia paralytica into one of dementia praecox of the catatonic type. A question arises as to the relationship of dementia paralytica to dementia praecox. Was the first stage dementia paralytica and was the second one genuine schizophrenia? The serologic findings in the first are undoubtedly the decisive diagnostic factors, besides the characteristic somatic and mental manifestations. In the second stage one finds all the typical reactions in the mental and affective spheres to justify a diagnosis of the catatonic form of schizophrenia. One can therefore admit that my patient began his psychotic state with undoubted dementia paralytica and terminated with catatonia. The logical inference in such an occurrence is that fundamentally the patient had "latent schizophrenia" (Bleuler) but the lesional factors of dementia paralytica produced such psychic changes as to dissociate or split the psychologic groupings characteristic of such persons. The syphilitic meningo-encephalitis characteristic of dementia paralytica may be perfectly analogous to other infectious processes in the course of which one observes psychopathic disorders, such as typhoid, epidemic encephalitis, pneumonia and some other similar conditions.

Analysis of the personality characteristics of the patient reveals all the elements of a schizoid constitution. Isolation and interiorization, so to speak, are the chief features which could be seen in all his activities. When such a person is attacked by an infectious process, such as syphilis, the process will find a ready soil for disorganization or dissociation of the personality. This process will split up all the component elements and render the patient unfit to remain in contact with reality. In my case the dementia paralytic phenomena developed on a schizoid background, and as soon as the anatomic lesions were therapeutically attacked and improvement was obtained in the form of a remission the psychologic dissociation became profound and its phenomena more and more distinct. The splitting of the personality was eventually complete and total, and the patient entered finally into the schizophrenic state, which ordinarily is the ultimate termination in the life of

a schizoid person. The most elementary tendencies of his personality were no more under the control of consciousness, and their activity became similar to those of dreams.

This patient therefore presented two psychoses, one of which produced such profound anatomopathologic changes as to become a point of departure for a process of dissociation of the personality of an innate schizoid type and brought to the surface latent schizophrenia.

DISCUSSION

DR. FREDERICK H. ALLEN: There is no mental picture pathognomonic of dementia paralytica, so that one cannot say that a diagnosis of this condition carries with it any set behavior. Nor is dementia praecox an entity in itself, although it has been built up and is sometimes regarded as a distinct entity. Therefore it is a little misleading to speak of two psychoses coexisting when there is no pathognomonic picture for either one. The behavior of a person with dementia paralytica will be strongly influenced by the type of person he was before this condition began to develop. This was definitely shown in an unpublished study made of cases of dementia paralytica at Phipps Psychiatric Institute. In a large proportion of these cases, the behavior was a reflection of the person's previous personality. The expansive types frequently were the more outgoing, extroverted types of personality in their normal states; the person inclined to be depressed and anxious frequently responded with that kind of behavior. In other words, the behavior of the person with dementia paralytica frequently is an extension and exaggeration of his more normal reactions.

In the case which Dr. Gordon has presented there was a clear history of a shut-in, dreamy personality. This behavior picture was intensified when the changes characteristic of dementia paralytica began to undermine the organic structure. The behavior picture became that of a catatonic type of dementia praecox. But I think it is misleading to refer to this as one psychosis being superimposed on another.

There is need for more clinical research on this question, and a study of the preexisting personality traits of a group of persons with dementia paralytica and the relation of them to the behavior during the psychosis would be interesting. Maybe Dr. Gordon's interesting case might stimulate such a study.

DR. ROBERT A. MATTHEWS: Dr. Gordon's paper and the case which he has cited may serve as a basis for the discussion of the coexistence of psychoses in general and of the effect of the past personality on the type of mental reaction likely to develop in any potentially psychotic person and, in particular, on the type of reaction likely to be observed in a patient with dementia paralytica. It is well known that toxic factors frequently complicate organic or so-called functional psychoses, as exemplified by the cases recently reported by Levin wherein delirium or hallucinosis produced by the ingestion of bromides was superimposed on, modified or precipitated a chronic mental disease. Alcoholic intoxication, acute or chronic, is so frequently seen in other types of mental illness that it at times leads to an erroneous preliminary diagnosis. In certain of these cases one might be justified in asserting that two psychoses were operative in a single person. In dealing particularly with dementia paralytica, one can postulate four possibilities: (1) Dementia paralytica may simulate almost any other form of mental diseases; (2) it may reactivate a prior existing mental disease; (3) it may serve as a point of departure for a so-called functional psychosis, as suggested by Dr. Gordon, and (4) there may be a distinct change of dominance in the mental picture during the course of dementia paralytica. The first possibility is exemplified by the case of a white woman, aged 22, who at the time of admission to the Philadelphia Hospital for Mental Diseases was markedly catatonic, entirely mute and resistive. Response to tryparsamide therapy was rapid, and recovery is now almost complete. One can look on this case as one of dementia paralytica characterized by catatonic phenomena, the diagnosis being made on the basis of the history and serologic tests, which were characteristic. There was nothing in the patient's past personality

to suggest schizophrenia. A male patient who presented almost identical symptoms recovered completely under treatment and has made an excellent extramural adjustment.

An example of the second possibility mentioned is the case of a white man who experienced a schizophrenic reaction type of mental disease in 1913. After being hospitalized for almost three years he recovered sufficiently to be paroled. He was able to make an economic extramural adjustment until 1932, when dementia paralytica developed and necessitated rehospitalization. The course since then has been progressively down-hill in spite of extensive therapy. The mental picture which he presents is that of hebephrenic dementia praecox, manifested by extreme silliness, vague hallucinations, echolalia and echopraxia.

As a possible example of the third group may be cited the case of an introverted white woman, now 22 years of age, who contracted syphilis from her husband at the age of 17. This worried her greatly, and she began to avoid acquaintances, gradually becoming more and more seclusive until, a few months ago, catatonic phenomena developed which necessitated hospitalization. The serologic reactions were characteristic of dementia paralytica, and one might consider that this disease served as a point of departure for the schizophrenia, as suggested by Dr. Gordon in his case, but, on the other hand, the psychic trauma produced in this introverted person by the knowledge that she was suffering with a venereal disease may have been a more important etiologic element. This is further substantiated by the fact that in spite of extensive treatment the condition has remained essentially the same.

The fourth possibility is represented by the case of a middle-aged man, who when first hospitalized was hyperactive, aggressive and grandiose. The condition appeared to improve for a time, but after eight doses of tryparsamide a rather severe but temporary amblyopia developed. During this period the patient became very quiet but exceedingly hostile, and there developed definite paranoid delusions. This episode was superseded by a period of marked depression, which in turn gave way to an almost complete remission. The patient was subsequently paroled, and when last heard from was in a fair state of mental health, but tabetic signs were developing. Within a year's time, this patient presented three distinctly different mental pictures.

In Dr. Gordon's patient there may have been merely a change of dominance in the mental symptoms with some intellectual deterioration produced by the dementia paralytica and not a true schizophrenia, since the remission was of short duration and there is little evidence that the paretic process was actually controlled.

DR. ALFRED GORDON: Dr. Matthews spoke of the simulation of dementia praecox by dementia paralytica. All neurologists are familiar with that to a certain extent. For instance, schizophrenic persons may have hallucinations, and so may persons with dementia paralytica. There may be episodes of euphoria and exaltation in both conditions, and analogous delusions may be present. But that does not negate the possibility of having clearcut cases. The person with dementia paralytica must not necessarily have a schizophrenic make-up, since the former is an incidental disease which any one may develop. In the present case, there were two distinct periods. One was typical dementia paralytica, if one relies on the neurologic signs and the psychiatric symptoms. After the period of remission, one could not escape from making a diagnosis of dementia praecox. There are cases which simulate dementia paralytica to a certain extent, but the symptoms are not typical or classic. Dr. Matthews suggested that perhaps there was a change of the psychotic picture. The point I particularly wish to emphasize is the damage produced in the brain by dementia paralytica. Since schizoid persons may not become schizophrenic, my patient might have passed through life without trouble had it not been for the cerebral trauma, which caused an exacerbation of the natural tendencies which the boy had carried from infancy.

THE FEELING OF UNREALITY AS A DIFFERENTIAL SYMPTOM OF MILD DEPRESSIONS. DR. JOSEPH C. YASKIN.

This article will be published in full in a later issue of the ARCHIVES.

THE PSYCHOPHARMACOLOGY OF SODIUM AMYTAL. DR. MELVIN W. THORNER.

A review is made of the different theories concerning the mode of action of sodium amytal. The suggestions of Bancroft and of Bleckwenn are outlined, together with the ideas of some of their followers and critics. Different factors pertaining to the dosage and mode of administration are mentioned. A Babinski response is reported in nine patients to whom the drug was administered intravenously. The reactions to the intravenous injection are set forth and discussed. It is suggested that oral administration of sodium amytal before its intravenous use will lengthen the period of unconsciousness. The reactions of patients in the various psychotic groups to the drug are discussed symptom by symptom.

The conclusions reached are as follows: 1. Sodium amytal produces marked mental changes in some patients suffering from abnormal mental reactions. 2. Its action seems to be largely that of an anti-inhibitory agent, although it is probable that there are other actions on the nervous system. 3. The anti-inhibitory action may occur through depression of the activity of some of the neurons of the cerebral cortex. 4. In certain psychotic reactions the changes produced by sodium amytal are undesirable from the therapeutic standpoint.

DISCUSSION

DR. E. V. EYMAN: I wish to add one point because of some of the work I have done with sodium amytal. In addition to the mechanisms Dr. Thorner mentioned, I think that there is another. I noticed that the group of men who first started the work with sodium amytal at the Pennsylvania Hospital secured excellent results, better, in fact, than have been obtained since. Those men spent much time with the patients. They were with them a great deal, eliciting information and talking with them, when the patients were in the semihypnotic state. Then another group of men took over the work. There were practically no results. These men spent much less time with the patients. More recently, under still another group of physicians, there have again been better results. I think that the suggestibility of the patient during narcosis may have some bearing on the results that are obtained and on the variability of the results.

DR. ALFRED GORDON: The remarks of Dr. Eyman are valuable. He made it emphatic that his patients were observed under intramural conditions. I want to say something about extramural cases. I have found that in all such cases sodium amytal is one of the best sedative drugs for use in agitated conditions. In the case of four patients whom I have under observation at the present time sodium amytal is practically the only thing that keeps them in a quiet state and gives them sleep.

DR. S. T. GORDY: Dr. Eyman hit the nail on the head in comparing the results obtained with sodium amytal in the Pennsylvania Hospital by two separate groups of workers. Not only sodium amytal but any drug which brings the patient into more frequent contact with his physician is useful. A whole group of drugs, among which are sodium amytal, alcohol and other similar agents, are presumed to have a selective affinity for the central nervous system. Today it is customary in studying their action to append the word "psycho" to the study of the pharmacologic action. Not so long ago Hugo Muensterberg revived an ancient psychologic notion and used the term "psychophysical parallelism." The notion was that the psyche and the body are parallels and that therefore "never the twain shall meet." It appears that with studies such as the one presented tonight, using agents which have this so-called selective affinity, the parallel twain do meet. Sometimes one starts out to find one thing and finds another. The value of studies such as these are not only that they apparently throw more light on the patients subjected to study but that they throw more light on the drug used. Furthermore, the bridging over of the supposed separation between body and mind by the use of these agents has another value. It tends to break down the artificial separation between the

so-called organic and the so-called functional as applied to disease processes. This, I believe, is of great importance.

DR. F. H. LEAVITT: Did the patients suffer any ill effects from taking this drug? At a recent meeting of the Philadelphia Neurological Society I reported a case of amytal poisoning. In discussing my case, Dr. Hadden reported two deaths as a result of the use of amytal. Were there similar untoward results in any of these cases? The drug under discussion in my presentation was amytal compound (amytal with amidopyrine) and not sodium amytal.

DR. ROBERT A. MATTHEWS: I wish to clarify Dr. Leavitt's statements concerning the untoward effects observed by himself and Dr. Hadden following the administration of amytal with amidopyrine or amytal, especially when used in combination with morphine. In their cases sodium amytal was not at fault. I think that it will be found that it is true that in cases in which toxic effects have been noted, either amytal or amytal with amidopyrine was used, not sodium amytal.

DR. L. H. SMITH: Sodium amytal is not in wide usage as yet, and so far not many presentations of papers have been brought out showing what complications might arise. What I have been interested in particularly in extramural work has been the possible toxic effects of any of the sedatives in use. In the past difficulties have often appeared in connection with different medications. When allonal (a barbital derivative with amidopyrine) was first used there was a good deal of discussion about its possible toxic effects, but, on the other hand, these so-called toxic effects were thought to be due to personal or physiologic idiosyncrasies.

With amytal or sodium amytal undoubtedly such idiosyncrasies exist in many cases, but experience seems to be pointing out that they are much less frequent than with many other sedatives.

DR. HAROLD D. PALMER: Dr. Matthews has already brought up the question which was raised in my mind by Dr. Leavitt's statement regarding certain toxic manifestations after the use of amytal. I have repeatedly given large doses of sodium amytal intravenously, intramuscularly, by mouth and by rectum without apparently approaching a lethal dose. It has not been at all uncommon during the course of the narcosis treatment at the Pennsylvania Hospital to administer as much as from 150 to 200 grains (9.7 to 13 Gm.) of sodium amytal in twenty-four hours. So far in our series of approximately fifty cases my associates and I have observed no untoward reactions. However, with the barbital and amidopyrine compounds toxic reactions are not uncommon. Recent literature calls attention to the barbital-amidopyrine compounds as possible etiologic agents in agranulocytic angina.

DR. MELVIN W. THORNER: I realize that this work might be criticized on the grounds of a concomitant psychologic influence on the patients. To this end, patients were left alone as much as possible. The capsules of sodium amytal were given by the nurse or attendant, and the patients were observed from afar.

The recent article by Malamud and Lindemann in the *American Journal of Psychiatry* (**13**:853 [Jan.] 1934) contains some interesting studies on patients to whom sodium amytal as well as other drugs were administered. In Dr. Brill's discussion of this article, I gather that talking to a mute patient might be as effective as the administration of intoxicating drugs.

No untoward reactions to the drug occurred among the patients in this series, but there never was more than 7½ grains (0.49 Gm.) given intravenously, unconsciousness always being produced with that amount. Oral premedication with sodium amytal has proved helpful.

Judging from its action in the outspoken psychoses, I suspect that its use for extramural catatonic and negativistic patients tends to establish better rapport between patient and physician and counteracts any tendency toward antagonistic moods.

It is often necessary to give large doses before giving up the use of the drug. In one case I found a sufficient dose to be 1 drachm (3.9 Gm.) three times a

day for several days without any untoward reaction. On the other hand, I have seen a cutaneous reaction resembling a phenobarbital rash after one capsule had been given. This subsided spontaneously.

Many patients to whom sodium amytal is given manifest symptoms simulating alcohol intoxication. This result is frequently a desirable one and may be considered what Bleuler termed "seminarcosis."

In common with some of the previous discussers, I have found amytal definitely more toxic than sodium amytal. I see no reason to use the former in neuropsychiatric states. In most of the instances of untoward reactions amytal was administered.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

March 15, 1934

ALBERT W. STEARNS, M.D., *Presiding*

ACUTE SYPHILITIC MENINGITIS. DR. MERRILL MOORE.

For a number of months, under Dr. Solomon's direction, Dr. Merritt and I have been studying some of the clinical problems of neurosyphilis. Although acute syphilitic meningitis has been known for many years and there are numerous articles on this subject in the medical literature, only the studies of Rothschild and of Moore offer any information as to the ultimate results in this condition. Therefore, we have endeavored to study the patients with acute syphilitic meningitis who were admitted to the Boston City Hospital, the Massachusetts General Hospital and the Peter Bent Brigham Hospital in the last fifteen years. We were able to find 80 well authenticated cases, in 24 of which examination was performed by us personally. This number indicates that the condition is relatively rare; Moore found it in 0.2 per cent of 2,600 cases of early syphilis, whereas Finger found it in 9 per cent of 500 early cases. The actual incidence lies somewhere between these estimates, probably nearer the figure given by Moore.

The ages of the patients in this series varied from 12 to 56 years, the majority being in the group from 19 to 39 years. There were two cases of congenital syphilis in the series. In two thirds of the cases acute syphilitic meningitis developed within one year of the primary infection; in the remainder of the cases the condition developed in from one to twenty years after the primary infection. The sex incidence was as follows: males, 48, and females, 32.

The treatment prior to the onset of meningitis had been varied. In one third of the cases the patient had had no previous antisyphilitic treatment; in the others meningitis developed during a lapse of treatment, with the exception of three cases in which it developed while the patient was receiving intramuscular injections of mercury. In none of the cases did the acute syphilitic meningeal reaction develop while the patient was being treated with arsenical drugs and bismuth.

The symptom complex depends largely on the chief site of meningeal involvement, and on this basis the cases may be divided into three groups.

Group I (26 cases).—The symptoms were chiefly those of a rapidly developing hydrocephalus, i. e., headache, nausea and vomiting, associated with symptoms of meningeal irritation. Neurologic examination in these cases showed only choked disk and stiffness of the neck. We have designated this group as cases of acute syphilitic hydrocephalus, or a simple pressure (increased intracranial) syndrome, associated with syphilitic infection of the meninges. We offer the hypothesis that these symptoms are due to a disturbance of the circulation of the cerebrospinal fluid by meningeal inflammation, mainly in the posterior fossa.

Group II (20 cases).—The symptoms were associated with involvement of the meninges over the vertex of the brain, i. e., headache, nausea and vomiting, con-

vulsions, mental disturbance and focal symptoms such as aphasia and hemiparesis. This group is considered as cases of a type or syndrome of vertical meningitis, on account of the concurrence of syphilitic infection, signs of meningeal irritation and symptoms of involvement of the vertex of the brain.

Group III (34 cases).—The symptoms consisted chiefly of palsy of the cranial nerves in addition to headache, nausea and vomiting, and to signs of meningeal irritation occurring in the course of syphilitic infection. The palsy was most often confined to one side of the brain stem, and the seventh and eighth cranial nerves were most frequently involved. Following these in order of frequency were the third, sixth, fifth and second nerves. These cases may be designated as the basilar group.

From the clinical aspect the three syndromes were remarkably well defined; only two cases showed evidence of combined vertical and basilar involvement. The vertical and basilar groups are already familiar in medical literature; the acute syphilitic hydrocephalus group is offered as a new entity.

The serologic findings in these cases are important; lumbar puncture is necessary to establish a diagnosis since we found the Wassermann reaction of the blood to be unreliable; it was negative in 40 per cent of the 80 cases. The cerebrospinal fluid showed remarkably consistent abnormalities: the pressure varied from 80 to 520 mm. of cerebrospinal fluid, and was over 200 mm. in 70 per cent of the cases; the cell count varied between 2 and 2,000, and in the majority of cases was between 100 and 1,000; in only one case was it less than 10 cells. The cells were chiefly lymphocytes, but polymorphonuclear leukocytes were present in some fluids. The colloidal gold reaction was abnormal in all but 3 cases, and showed first zone (dementia paralytic) curves in 40 per cent; the Wassermann reaction was positive in 86 per cent of the 80 cases.

The results of treatment in acute syphilitic meningitis are striking. There was 1 death, as a result of a decompression operation. The other patients were treated in the hospital by intravenous injections of an arsenical drug (in some cases intraspinous treatment was given), in addition to lumbar puncture and rest in bed. In approximately twenty-one days the majority of the patients were discharged from the hospital entirely relieved of symptoms.

We have been able to follow 38 of these patients for periods varying from two to sixteen years. Of 26 patients who received standard treatment, 80 per cent were symptom-free and had negative serums at the end of this period of observation. Of the 6 patients who received substandard treatment, only 1 showed complete clinical recovery and normal serum at the end of the period of observation.

On one hand, the results of our study disprove the claim of Mattauschek that an attack of syphilitic meningitis protects the nervous system from later parenchymatous involvement; on the other hand, our results indicate that the ordinary routine or standard treatment in these cases with arsenical drugs (arsphenamine) can prevent the development of late neurosyphilis.

SYPHILIS OF THE SPINAL CORD. DR. HOUSTON MERRITT.

I shall present a preliminary report on a study now in progress on forms of disease of the spinal cord due to syphilis other than tabes dorsalis. Pure syphilis of the spinal cord is relatively rare. Erb placed its frequency as one tenth that of tabes, and Fournier found 77 cases in 416 patients with cerebrospinal syphilis. The age of incidence is not important, as it varies from 20 to 59 years. Males are affected about twice as frequently as females.

The symptoms may appear within a few months of the primary infection or as late as from twenty to thirty years. Approximately one third of the cases occur within one year after the infection. The previous therapy in the majority of these cases was substandard, and in over one third of the cases there was no history of previous treatment.

The symptomatology and clinical syndromes are related to the peculiarities of the anatomic structure of the spinal cord in that a small lesion can produce special

symptoms. The symptoms are due to involvement of the meninges and of the blood vessels. The term myelitis is commonly used, but the actual inflammation present is restricted usually to the meninges and to the walls of the blood vessels.

The clinical syndromes of syphilis of the spinal cord (exclusive of tabes dorsalis) can be divided into three groups: (1) meningomyelitis; (2) thrombosis of the spinal arteries, and (3) chronic anterior poliomyelitis.

In the first group, the symptoms have a slow or subacute evolution and depend on the location and the nature of the meningeal involvement. If the inflammation is of a nonspecific (not gummatous) character, the pathologic changes will be confined to the nerve roots and the circumferential areas of the cord, causing pains in the spinal nerve roots, muscular weakness, disturbances of the bladder and a spastic paralysis, with hyperactive reflexes and Babinski's toe sign, without a definite sensory level. If, however, the meningeal reaction is specific, i. e., with gummatous formation, a compression of the cord may result, and the symptoms will be similar to those produced by any tumor of the spinal cord.

In the second group the symptoms are usually of sudden onset and reach full development within a few hours after the onset. Premonitory symptoms, such as pains in the nerve roots, weakness and paresthesias, may appear, since thrombosis often occurs in the presence of a preexistent meningitis of the spinal cord. The clinical syndrome is usually that of an acute transverse lesion of the cord, with flaccid paralysis below the lesion (usually middorsal) and loss of control of the bladder and the rectal sphincter.

In the third group the symptoms are those of chronic progressive atrophy of the muscles of the upper or lower extremity, due to degeneration of the anterior horn cells. The pathologic changes in these cases may be due to endarteritis of the vessels of the spinal cord with resulting ischemia of the ventral horn cells, or to primary involvement of these cells without any evidence of vascular disease.

The serologic findings in these cases depend on the degree and the nature of the meningeal involvement. If there is an acute meningeal inflammation the cerebrospinal fluid is markedly abnormal, but if the symptoms are due to thrombosis of diseased vessels the cerebrospinal fluid may show relatively few changes. When the meningeal involvement is of the gummatous type, spinal subarachnoid block may be present.

The results of therapy are variable. It is difficult to foretell how much recovery may be expected. The degree of recovery depends, first, on the extent of degeneration that has already occurred and, second, on the nature of the pathologic process producing the symptoms. Good results may be expected in cases of meningomyelitis when the process is of relatively short duration and the symptoms are due to acute meningeal inflammation. Poor results may be expected in cases in which extensive damage has already occurred, or when the symptoms are due to myelomalacia from thrombosis of the spinal arteries. In the last type of cases, death often results from septicemia or cachexia associated with extensive bed sores.

THE TREATMENT OF DEMENTIA PARALYTICA. DR. HARRY C. SOLOMON.

In February 1934, on analysis of the results obtained in a group of 173 patients suffering from dementia paralytica who were treated by inoculation with malaria organisms between February 1925 and February 1931 and given other treatment as well, it was found that a thoroughly good improvement, from the clinical standpoint, was obtained in 36.4 per cent and a definite improvement in 25.1 per cent. The serologic results in 169 of the patients who could be followed subsequently indicated a completely negative spinal fluid in 36.7 per cent, a greatly improved fluid in 20.7 per cent and some improvement in the fluid in 18.3 per cent.

As a result of the analysis my colleagues and I are ready to state that dementia paralytica can be arrested in a great majority of cases if treatment is instituted before the disease has progressed too far, and if the general physical condition of the patient, outside of the involvement of the central nervous system, is suffi-

ciently good for him to receive the rather radical treatment and allow for a reasonable length of life. This statement is based on the facts that a negative spinal fluid is obtainable in the course of years in such a large percentage of cases, that the life expectancy is increased by years and that the progress of the mental disease is arrested.

If one considers only the final clinical state of the patient there will be many disappointments. This, we believe, is because the irreparable ravages of the spirochetal infection have already gone far in many of the cases before treatment was instituted. The best method of treating patients with dementia paralytica cannot be determined, in our opinion, at the present time. In our series of cases, various forms of treatment were given in addition to the malaria in a large percentage of the cases. Such treatment consisted of injections of drugs, particularly tryparsamide and arsphenamine, as well as the administration of bismuth, mercury and the iodides by mouth, and also the induction of fever by sodoku, typhoid vaccine, injections of milk and diathermy. It is our distinct impression that a combination of other methods in addition to the malaria gives more satisfactory results than malaria alone.

RECAPITULATION OF THE PRECEDING PAPERS. DR. HARRY C. SOLOMON.

In recapitulating the material of the three preceding presentations one may draw definite conclusions regarding treatment for syphilis of the central nervous system. Acute syphilitic meningitis responds readily to antisyphilitic drugs, and when these are continued for a reasonable time (at least from one and a half to two years, or preferably for several years) the prognosis is good. Even when the parenchymatous tissue is invaded by the spirochete, as in dementia paralytica, a complete arrest of the disease may be expected under proper treatment.

The final prognosis in many cases depends on the amount of damage that has occurred before the activity of the pathologic process has been therapeutically arrested.

The results of treatment in the tabetic form of neurosyphilis are similar to those obtained in dementia paralytica, although in many instances improvement may be achieved by less intensive therapy. Although an arrest of the pathologic process is to be expected, the functional capacity of the patient will be largely dependent on the damage to the parenchymatous tissue which has occurred. In the group of cases in which vascular disease is responsible for the symptoms, actual damage to the tissue is likely to have resulted, which damage is irreparable. How far an arrest of a degenerative process in the vessels can be accomplished in still *sub judice*.

In conclusion, it may be stated that the present methods of treatment afford an opportunity for the arrest of various types of syphilitic involvement of the central nervous system, whether these are meningeal or parenchymatous. The past twenty years have brought a complete revolution in thought concerning the prognosis in neurosyphilis.

DISCUSSION

DR. K. J. TILLOTSON: In several clinics abroad and in the Wagner-Jauregg clinic, Dr. Dattner has been treating patients with dementia paralytica with malaria therapy. As Dr. Solomon has noted, the progress of the disease when the treatment is instituted determines the success of the therapy. I think that in the more advanced psychotic cases the percentage in the Vienna clinic is about the same as Dr. Solomon has found. Panze treated 1,500 patients with dementia paralytica and syphilis of the central nervous system and when I questioned the typical diagnosis he said that the conditions were not always advanced; some patients had only colloidal gold reactions or slight neurologic or personality changes. Panze has had great success with fever therapy. I wish to ask Dr. Solomon if he has followed these cases in which fever therapy and no tryparsamide was used, and compared them with cases which tryparsamide alone was used. It seems that the earlier institution of fever therapy might save a great deal of time.

DR. H. R. VIETS: Dr. Solomon and his co-workers have aided in the revolutionization of this subject which has taken place in the last twenty years, and Dr. Solomon himself must be considered as one of the pioneer workers. It is easy to accept a program of this character in 1934, without particularly inquiring into its significance. In 1914, such a lecture would have been impossible, for no one at that time considered the future treatment of patients with dementia paralytica except with great pessimism. As soon as the diagnosis was made most patients were sent to state hospitals for mental disease. One was always surprised to learn that a patient was alive a year after entry, and if a patient lived into the second or third year it was considered an event of unusual interest. In this community, at least, Dr. Solomon has led the way in changing all this, for he is now able to report that over half of his patients with dementia paralytica are working from three to ten years after the diagnosis was made.

The attitude in general, moreover, toward all types of neurosyphilis is greatly changed. When one sees a patient today, one expects to stop the activity of the disease and in many cases "put the fire out" entirely. In cases of syphilitic meningitis this is particularly true; from 90 to 100 per cent of the patients are permanently cured of the active disease when properly and thoroughly treated. In other types of neurosyphilis the percentage is not quite so high; there are, moreover, the results of the disease itself, apart from the activity of the specific organisms. The scar left by an active process in the spinal cord may cause the patient to be seriously crippled even after the disease is cured. This is particularly true in one type of neurosyphilis not mentioned by the speakers, namely, atrophy of the optic nerve. I think that this is perhaps the most difficult of all types of neurosyphilis to treat, for rarely is one able to stop the activity of the disease before vision is practically gone.

DR. T. J. PUTNAM: There are one or two points about which I wish to ask. Will Dr. Solomon or one of the group lay more emphasis on differential diagnosis. Of course, what I am thinking of most is the question of increased intracranial pressure as it hits my own field of cerebral tumors. I wish to press Dr. Solomon to give his impression of the relative advantages of malaria treatment as compared with physical hyperthermia treatment. Dr. Solomon mentioned some deaths due to malaria, and I wondered if these could be diminished by some form of fever which was not pathologic.

DR. A. BERK: I worked with Dr. Solomon from 1925 to 1930, and I feel that I have had a hand in most of these cases. There are two things I wish to stress: One should send these patients to Dr. Solomon earlier. Von Jauregg mentioned that if he could see the patients earlier, he could get 100 per cent of cures. These patients of Dr. Solomon's have been really treated; I know one who has been under treatment for over eight years.

DR. H. R. VIETS: Neurologists are all coming to realize that the dementia paralytic colloidal gold curve, so-called, does not by any means always indicate the presence of dementia paralytica. Such a reaction may appear in many types of neurosyphilis, particularly if the patient has not been previously treated. The value of the colloidal gold curve is largely one of prognosis. When it remains dementia paralytica in type after from six months to a year of intensive treatment, it becomes a strong sign indicative of dementia paralytica. Another question concerns the value of treatment in the "burnt-out" cases. I think that certainly many patients derive definite benefit from short courses of intravenous treatment, given at periods of about once a year, even though the blood and spinal fluid have become entirely normal.

DR. J. LOMAN: It is interesting to contrast old methods of treatment with the methods reported by Dr. Solomon and his co-workers. In a study of records of patients with dementia paralytica who were at the Boston State Hospital from 1920 to 1930, it was found that the percentage of remissions in the treated group was only about 3 per cent greater than that in the untreated group.

DR. W. BLOOMBERG: How high a total protein content has been seen in the cases of acute syphilitic meningitis?

DR. A. W. STEARNS: In olden times, it is said, one of the things which a medical student had to learn was to comfort the bereaved. Those of us who were in the state hospital service twenty years or more ago had a similar conventional duty in consoling the families of those persons whose condition was diagnosed as dementia paralytica. It is gratifying to hear so much optimism expressed.

DR. H. H. MERRITT: In answer to Dr. Bloomberg's question, the total proteins ranged from a low normal of 30 to 361 mg. per hundred cubic centimeters. As to Dr. Putnam's question, the differential diagnosis of tumor of the brain and also of abscess of the brain is difficult, as the symptoms are much the same. The persons in the group with acute syphilitic hydrocephalus have only the symptoms of headache, vomiting, etc. Choked disks are seen on examination, and in many clinics, because of the choked disks, a lumbar puncture is not done. The patients are subjected to an exploratory craniotomy, and a diagnosis of arachnoiditis may be made. Examination of ventricular fluid in such cases is not satisfactory, since the Wassermann reaction of this fluid is often negative when that of the lumbar fluid is strongly positive. The differential diagnosis between basilar syphilitic meningitis and neuroma of the acoustic nerve is often difficult, since the angle nerves (sixth, seventh and eighth) may be involved in either. In neuroma of the acoustic nerve the evolution of symptoms is slow and the involvement of the eighth nerve precedes that of the other nerves in most cases. In doubtful cases examination of the spinal fluid is necessary for a diagnosis, since the Wassermann reaction of the blood is negative in 40 per cent of cases of syphilitic meningitis. The danger of lumbar puncture in cases with choked disks is small if proper precautions are taken.

DR. HARRY C. SOLOMON: Dr. Tillotson brought up the question of fever treatment in early syphilis. It seems to me that it is not necessary if proper treatment is given. The Austrian point of view is that fever therapy should be given in early cases because the patient may not have the right attitude toward treatment and may leave before he is adequately taken care of. Dr. Yorshis asked about the personality changes and prognosis. All I can say is that patients who come in with a more or less schizophrenic syndrome have a very unfavorable prognosis. My co-workers and I have not treated patients solely with malaria, because we believe that we get better results with the combined treatment. At the Psychiatric Institute, New York, Kirby and Bunker carried out their treatment with malaria alone; the remissions in their cases were 21 per cent as compared with 37 per cent in our group. A good many European workers have used only malaria and have reported up to 40 per cent remissions. I am glad that Dr. Viets spoke of the previous pessimistic attitude. This afternoon I was talking with a man who said, "We will never know anything about the emotional psychoses, never." That is what was said twenty years ago about dementia paralytica. I have had relatively few cases of atrophy of the optic nerve in which malaria therapy has been used. I think that there have been some cases in which the condition has been arrested. I avoided discussion of diathermy or other methods of producing fever. I hope to report results with diathermy at a later date. My present feeling is that results are not so good as with malaria.

EXPERIMENTAL STUDIES IN ALCOHOLISM: THE ALCOHOL CONTENT OF THE BLOOD AND CEREBROSPINAL FLUID FOLLOWING ORAL ADMINISTRATION IN ABSTAINERS, CHRONIC ALCOHOLISM AND THE PSYCHOSES. DR. ROBERT FLEMING and DR. ELMER STOTZ.

This article will be published in a later issue of the ARCHIVES.

PHILADELPHIA NEUROLOGICAL SOCIETY

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D. J. McCarthy, M.D., *President, in the Chair*

POSTENCEPHALITIC ARTHROPATHY OF THE TEMPOROMANDIBULAR JOINT. DR. ALFRED GORDON.

Epidemic encephalitis may be followed not only by sensorimotor, mental and emotional disturbances but also by a large number of disturbances of vasomotor and trophic character. This disease, therefore, in its chronic form, presents a favorable subject for the study of the vegetative centers of the midbrain, which is supposedly the chief anatomic seat of encephalitis. Among the neurovegetative manifestations, special attention is drawn here to arthropathies of an exceptional type and localization. The case presented shows early and rapidly developed deformities in the hands and mandibulotemporal articulations in a postencephalitic patient.

Arthropathies of the large joints have been observed infrequently in nonsenile persons in the group with parkinsonian symptoms, and arthropathies of the small joints have been observed still more rarely. As to mandibulotemporal involvement, there are apparently no records of it. Deformities exclusively of the fingers, with fixed contractures in which there was hyperextension of the first phalanges and flexion of the other phalanges, were seen in the case of Hall. In this case the rest of the body was not involved (La dégénérescence hépato-lenticulaire; maladie de Wilson, pseudo-sclérose, Paris, Masson & Cie, 1921, p. 54). Association of classic paralysis agitans with typical chronic rheumatism is not an infrequent occurrence, as they both occur usually in advanced age, and Charcot insisted on the analogy between these deformities and chronic rheumatism, but articular disturbances in the course of postencephalitic parkinsonism are rather rare. If they occur, they are limited to one or two symmetrical joints and consist of fixation or ankylosis without enlargement or thickening of the articulating bony tissue, such as is seen in arthritis of rheumatic origin. The pathogenesis of articular deformities has been the subject of research by many investigators. Such a course of events is the opposite of what one observes in articular rheumatism of the deformans type. Mingazzini spoke of the striatum having a trophic function; Marinesco placed the pathologic factor of postencephalitic arthropathies in Luys' body, in the pallidum and in the tuber cinereum, all indicating the existence of many vasomotor centers in the midbrain, the function of which is to keep under control the vegetative centers. One is also bound to bear in mind the accumulated data concerning investigations on the chemical side of the postencephalitic syndrome, which may play a certain rôle in the trophic disorders under discussion.

Disturbances in the function of the endocrine glands also claim a certain causative rôle in trophic disorders of various tissues.

Taking into consideration all these various sources for the production of dystrophies, one may take the position with the physiologist Foà that the mechanism of coordination and regulation of organic functions is not only nervous, endocrine or humoral, but that there is probably an interrelation between all these factors (*Rassegna di clin., terap. e sc. aff.*, 1911, vol. 10, no. 5).

The rich history of various disorders occurring in the postencephalitic life of a person with parkinsonian symptoms, including the arthropathies considered in the case presented and the mode and date of development of those additional disorders lead to the thought that the activity of the encephalitic process does not terminate with the symptom group of parkinsonism, that the latter is far from being a perfectly stabilized morbid manifestation and that probably the anatomic changes may be for a long time only of an irritative character but later become destructive.

The case under consideration is an example of parkinsonian arthropathy in an exceptional locality, which is pathogenically associated with the unstabilized chronic postencephalitic process.

ASSOCIATED MOVEMENTS OF THE TONGUE IN EPIDEMIC ENCEPHALITIS CONTROLLED BY VOLUNTARY EFFORT. DR. MELBOURNE J. COOPER.

This article will appear in full in a later issue of the ARCHIVES.

PNEUMOCRANIUM IN THE TREATMENT OF TRAUMATIC HEADACHE, DIZZINESS AND CHARACTER CHANGE. DR. WILLIAM DRAYTON JR.

This article appears in full in this issue of the ARCHIVES, page 1302.

THE GROWTH OF THE SPINAL CORD IN RELATION TO REFLEX ACTION. DR. G. E. COGHILL (from the Wistar Institute of Anatomy and Biology, Philadelphia).

The embryologic approach to the problem of cortical localization, according to the principle of relative acceleration of growth in definite foci, clarifies some of the obscurities and contradictory views concerning the function of the cortex. Lashley and others found a minimum of localization of function in the cerebral cortex of the rat and a maximum of action of the cortex as a whole in the sense of equipotentiality. In this respect the cortex of the rat is like the spinal cord of Amblystoma when the localized functions of the leg begin to appear. The spinal cord at this time still performs its general integrative functions for the body as a whole, but under appropriate conditions can perform a local function. This local function is first a simple movement of the leg as a whole; later knee action, foot action and toe action become differentiated or individuated. Similarly, progressive localized acceleration in the cerebral cortex gives rise to various degrees of localization of function according to the species. In the oppossum, for example, a center nerve appears which is localized to the hindleg. But the important consideration is that localized cortical mechanisms arise within a general mechanism of integration. The topographically localized cortical center must not be thought of as performing exclusively localized function, for it exists in a field of general function. This is illustrated well by the recent work of Jacobsen and Fulton on cortical functions in lower primates. There is in these forms a localized center of specific control over movements, but bordering this center is a region which influences motor functions in a general way but without specific control. In other words, the entire motor area does not have localized control over movement. All the cortical motor area should be thought of as having a general relation to motor functions, while only a part of it acquires specific relation to muscle groups. This part is prescribed by localized acceleration of growth relative to the rest of the area. One feature of this acceleration is the development of Betz cells. In the development of the cerebral cortex, as in the development of the spinal cord, in relation to localized function, there come to be large numbers of small cells and a relatively few large ones, while in both localities it is the large cells which assume localized, specific functions. Furthermore, it is an important consideration that in development cortical motor centers rise into action in the same order as motility develops in the organs which those cortical centers respectively control. Why this should be is a mystery; but it is scarcely more mysterious than why a local growth of mesoderm, which is destined to form the leg, should initiate in the spinal cord those processes of growth which eventuate in that localized center which controls the leg.

Finally, as a general conclusion from my observations on the development of the nervous system in relation to its function it may be said that the growth of the nervous system proceeds according to a definite mode, which consists in the extension of a primarily integrated matrix in which localized centers of special function arise progressively by relative acceleration of growth in restricted parts. In this manner there arise the motor centers of the spinal cord and brain, the cerebellum, the centers of association in the thalamus, the basal nuclei of the forebrain, the archipallium, the neopallium and the localized motor centers of the cerebral cortex. Functionally, any or all of these centers may temporarily be submerged in the action of the integrated matrix as a whole, but when a localized center rises into action it acts normally under the influence of the whole.

Book Reviews

Social Psychology. By Abraham Myerson. Price, $3.50. Pp. 640. New York: Prentice-Hall, Inc., 1934.

A commonly accepted definition of the term social psychology is, according to Allport, "the study of the social consciousness and the social behavior of the individual." From this statement it is obvious that the extent of social psychology as a division of knowledge is wide and that in such a field workers of many kinds may report their findings with validity. Abraham Myerson is one of these workers and is a physician. He brings a new point of view, that of a man specially trained and interested in neuropsychiatry, with the special experience that this branch gives to the somewhat theoretical and academic attitudes that have made up what has been taught as social psychology by Professor MacDougall and others.

There is probably no physician in America whose social-medical experience exceeds that of Dr. Myerson. From this background and out of his own experience and study he has prepared a considerably revised formulation of what social psychology is and one that is obviously characterized by new considerations, fresh emphases and original points of view. After its title "Social Psychology," this book might well bear the subtitle "A Treatise on This Subject of Special Interest to Physicians."

The book is arranged in twenty-one chapters, but first there is an author's preface that contains the key ideas that Dr. Myerson develops in detail later in his text. In addition, the book contains an index of authors and subjects, which facilitates the use of the volume for purposes of reference. The contents of the book are so various as to be almost disconcerting, but in handling this problem the author has subjected his material to severe condensation, and he has been successful almost to a fault. Behind the book, or seen through the book as though it were an aperture, plainly stand the important books of the past on social and psychologic topics. References to the literature lend the textual material added richness and to some degree relieve the condensation. Material that was irrelevant or repetitive has been eliminated, and the important and related features have been retained. On this account the book has a special sort of sequence of its own. It begins with the general problems and from them leads the reader to consideration of the social psychology of the family. The book ends with the topic "Misdoing." Any one who is familiar with Dr. Myerson's previous writings can appreciate the reasons why the family receives special attention in this volume. The chapter on the family is the best in the book. Considering its size, the book comes up to the standard set by Flügel in his more expanded treatise on this subject. Besides having the value of brevity, it has a certain simplicity that should recommend it to college undergraduates and students of psychiatric social work when they begin to orient themselves in that complicated region: the literature about the family, family life and the problems of the family.

Misdoing is discussed immediately after the family and its problems; this may be taken as indicative of Myerson's opinions about the hypotheses that relate delinquency and criminality to unsolved or badly solved problems in family life and the home. Myerson writes with no particular bias or prejudices. This is noticeably true in regard to the special theories and concepts of the psychoanalytic school. He is familiar with these, and he implies a serious appreciation of Sigmund Freud as a man, but, on the whole, psychoanalytic formulations are not given any position of special prominence. The book is written from a broadly humanistic point of view. From the foreword it is easy to see the attitudes that have come to have most meaning to the author. He states: "This book has been developed

from two main theses which justify my venture into the field of social psychology. The first is that the visceral-organic structure of man is basic to the understanding of psychology. . . . The second is that apart from his group man is a mere potentiality. He is developed in a milieu that fosters, modifies or destroys his capacities. And how that milieu works, the psychiatrist and physician has ample opportunity to witness."

Reduced to a formula, this means essentially that philosophically Dr. Myerson is an "organicist," though he is not merely that. He asks first for consideration of the visceral-organic basis of man, on which the other functions are superimposed. It may be said that Dr. Myerson's conservatism and saneness are somewhat unusual in this age of expanding theory. The book is full of concise and quotable passages. In his zeal and love of his topics the author has at times unconsciously admitted to his pages more beauty than one would expect from the textual content. In spite of its being a scientific text, the book contains a cry, a sort of message, a plea or a warning.

Dr. Myerson understands sex; the chapters that as well as any indicate his unusual understanding of human problems are those on sexuality (16 to 19). In dealing with this subject in its personal and social aspects he is so explicit and so observant that every one who is interested in himself should read these chapters and give them consideration. There are not many places where present day concepts of sexuality are so plainly condensed as here. It is a section of the book that the average practitioner should read himself and may well recommend to an intelligent patient.

Mental Hygiene and Education. By Mandel Sherman. Price, $2.25. Pp. 295. New York: Longmans, Green & Co., 1934.

Most psychiatrists and neurologists in America today are somewhat conservative and "organic"-minded, with the exception of a fairly small though articulate group who speak from a predominantly "functional" point of view. In this group are many of the most active and optimistic members of the profession, however, and some of them are looking hopefully toward nearby fields of knowledge and endeavor. Dr. Sherman apparently belongs to the latter group, and in this book attempts to call attention to the relationships, actual and potential, between the psychiatric and pedagogic professions. The cover of the book announces that it is a book *"planned to aid teachers to discover the emotional and personality problems of their pupils and to institute treatment."*

Whereas most neurologists and psychiatrists would regret to see such a practice as this carried out widely, it must be remembered that there is such a trend as this active in America today and that it must bear consideration. In a sense, it is the ancient problem of *layman versus trained-professional worker*, and though its origin is clear, no one can foresee the end. The reviewer himself believes that those who "discover emotional problems" and who "institute treatment" should be neurologically and psychiatrically trained physicians and not teachers who are interested in mental hygiene, but this must be admitted as personal bias if Dr. Sherman's book be given further representation.

Thirteen divisions and an index make up the contents. The titles of the divisions are: "Psychiatric Problems in Education," "Emotional Adjustment," "Personality," "The Manifestations of Personality," "Attitudes," "The Differentiation of Personality," "Conflicts," "Compensatory Behavior and Defense Reactions," "Phantasy," "Neurotic Behavior," "Symbolic Behavior," "Adolescence and Mental Disease" and "Conduct Disorders." These chapters contain a somewhat lucid, if not superficial, exposition of the concepts and phenomena listed, and fusion of them into an apparently unified presentation is effected. Associated reference notes support the tone of conviction which marks the author's style. One notes the lack of neuropathologic and neurophysiologic background in the greater part of the material presented. However, not to do a professional disservice to Dr. Sherman, it must be said in favor of his book that it has definite positive values

as well as the unfavorable points just criticized. Such books as this, books that urge an understanding of the emotional life of the student, are pioneers in a frontierless territory. The majority of teachers (with certain notable exceptions) have judged their classes as though they were homogeneous units, and in their attitude toward their teaching many have been (and are) stiffly pedagogic and oblivious of possible internal struggles in individual pupils; a work like Dr. Sherman's that proposes to relieve educational blindness is a manifest sign of educational advance.

Dr. Sherman is associate professor of educational psychology at the University of Chicago. His training in psychiatric research and his abundant educational experience make him capable of blazing a trail that teachers may follow, if they desire to educate their charges in a more psychologically informed manner.

The teacher will recognize in the descriptions of the timid child, the egocentric student and the hysterical pupil those types that he had perhaps classified as "obstinates." Now he may learn how to trace the causes, administer the proper remedies and orient these "incorrigibles" to the school environment. He will be slightly instructed in the art of psychoanalytic interview. Sample charts, tests and data sheets are provided to aid him in gathering information. That the school and home must be affiliated for complete understanding of the child's problem is adequately emphasized. The attitude of the child's family must sometimes be fundamentally changed if the child is to be helped. In the habits and in the ways of thinking of the parents the trained observer may discern the influences that condition the behavior of the child.

To the novice this book may well serve as an introduction to psychiatry. Theories about emotions, the development of the personality, the special ideas of Jung, Kretschmer, Freud and Adler, the factors which engender neuroses and the meaning of compensatory behavior are all listed and discussed.

The parent will discover that "to spare the rod is not to spoil the child." Observation has revealed that directions to children are most effective when accompanied by an explanation and not a threat.

Each chapter is followed by pertinent questions for discussion and select references, with the relevant pages noted. This feature makes the book of especial value to teachers, who will find it very interesting, but from the point of view of the practicing neurologist and psychiatrist the book is one that probably will be laid down with considerable doubt as to its fundamental value, for obviously it leaves much to be desired. If this book were one that simply pointed out to teachers the psychologic factors in pupils as phenomena to be considered, its value might be reasonably definite, but as it is a volume that in 295 pages undertakes to inform pedagogs "how to discover the emotional and personality problems of their pupils and to institute treatment," it may be regarded as silly, if not dangerous, in the eyes of experienced neuropsychiatrists.

Intercortical Systems of the Human Cerebrum. By Joshua Rosett, Assistant Professor of Neurology, Columbia University. Price, $3. Pp. 135, with 41 figures. New York: Columbia University Press, 1933.

This monograph represents some of the results of a serious and sustained attack on problems connected with the architecture of the association fiber systems of the human cerebrum. For following out the intercortical systems the author has devised a special procedure, which he calls automatic internal dissection. With this method a brain is placed in a steel container and subjected to a pressure of 1,000 pounds (453.6 Kg.) for one or two days. The valve is then quickly opened; this allows an internal explosion of the tissue. When the brain is examined it is found to be dissected along natural lines of cleavage. A study of these preparations shows that the intercortical fiber systems underlie the fissures and sulci and are lacking, for the most part, beneath the gyri. In addition, there are deep fiber sheets which are continuous beneath the bases of both the sulci and the gyri. These exist under the insula and in the region of the parieto-

occipital and calcarine fissures and also include what are usually called the arcuate fasciculus and the inferior longitudinal fasciculus. These sheets are probably vestiges of an ancient intercortical system which existed in the smooth or slightly fissured cerebrum. The basic microscopic structure of the intercortical systems is that of two sets of parallel bundles of fibers which cross each other at different angles, but this is often complicated by additional sets of fibers. The author's observation of the close association between the sulci and the intercortical pathways leads him to see a causal relationship between them and to suggest this relationship as an important factor in fissuration. He concludes that any particular pattern of fissuration must be considered the effect rather than the cause of the particular arrangement of the underlying pathways. The author is to be congratulated on the publication of this interesting study.

Anatomie médico-chirurgicale du système nerveux végétatif. By J. Delmas and G. Laux. Price, bound, 100 francs. Pp. 266. Paris: Masson & Cie, 1933.

The increasing importance of surgery of the sympathetic nervous system justifies the timely appearance of a monograph on this subject. It is subdivided into five chapters: histologic structure and systematization; the central vegetative nervous system; the central gray matter and pathways; the peripheral vegetative system; general systematization of the neurovegetative apparatus, and methods of surgical approach.

The last chapter (twenty pages), which is perhaps the most important to the practicing surgeon, is illustrated with eight excellent drawings, which compensate to a certain degree for the (intentionally) somewhat too short description in the text. The other four chapters (214 pages) give a detailed description of the anatomy and histology of the vegetative nervous system. The authors are always conscious of the fact that the antithesis, sympathetic-parasympathetic, is mainly a physiologic, and not an anatomic, conception. But in the text they adhere to the prevalent schemes as they have been worked out by Gaskell, Lashley and others. The reader will like the clear drawings illustrating the topographic anatomy of the different structures. Those interested in histologic details may complain of the lack of good photomicrographs of the different types of cells of the central gray matter and the peripheral ganglia. Others may criticize the somewhat hypothetic description of hypothalamic centers; but one should blame the present uncertain state of knowledge concerning these centers rather than the authors. In general, the book may be recommended as a welcome addition to the literature on the vegetative nervous system.

Die gerichtliche Schriftuntersuchung. By Rudolf M. Mayer. Price, 8.50 marks. Pp. 616, with 59 illustrations. Berlin: Urban & Schwarzenberg, 1933.

This book is a part of Abderhalden's monumental "Handbook of Biologic Methods." It deals comprehensively with the problems of expert examination of handwriting in its relation to criminology. Most of the book is devoted to a discussion of methods of detecting the identity of handwriting and determining whether forgeries exist in given specimens. Many indispensable mechanical aids, such as microscopy, special lighting and illumination and magnified photographs, are described in some detail. The chapter on the investigation of typewritten statements is based on Osborn's standard work ("Questioned Documents," 1929, second edition). There is a chapter on the pathology of handwriting, which takes up handwriting in schizophrenia, senility, epilepsy, alcoholism, dementia paralytica and other conditions. This section, however, is very brief.

For the forensic psychologist this book should prove of high importance. For the neuropsychiatrist who is interested in the neurologic analysis of movement and the diagnosis of abnormal and normal personalities, it deserves attention as a supplement to the larger textbooks on the subject.

Une nouvelle syphilis nerveuse; ses formes cliniquement inapparentes. By Paul Ravaut. Price, 45 francs. Pp. 196, with 3 plates in color. Paris: Masson & Cie, 1934.

Ravaut has been writing on neurosyphilis during the whole period of its scientific evolution, that is, for thirty years, and presents a number of interesting conclusions in this attractive volume. He deals particularly with the biologic form or latent or preclinical neurosyphilis, which is detectable only by examination of the spinal fluid. He points out the much greater success of treatment in the latent or preclinical forms than in forms that have gone on to definite neurologic manifestations. From the prognostic standpoint, the biologic reactions to syphilis are of considerable importance, positive reactions being danger signals, although negative reactions are not always to be relied on; partial reactions must be interpreted with care. It seems that negative reactions in the spinal fluid of a treated patient usually remain negative. Occasional unusual manifestations are bound to occur, so that absolute predictions cannot be made.

Ueber Ideenflucht. By Ludwig Binswanger. Price, 10 francs. Pp. 214. Zurich: Art Institute (Orell Fuessli), 1933.

This phenomenologic study attempts to explain flight of ideas not merely as a symptom but also as an expression of the attitude of the ego to the outer world. The leading factors in this highly complex phenomenon are the optimistic mood, the realization of the infinite scope of thinking, the restless speed of thinking, the volatility of the content of thoughts, the flowing of the various meanings into each other and the person's need to communicate with others. These are really the fundamental factors of the manic reaction. Their opposite is found in the depressions. This contrast is the characteristic feature of the manic-depressive personality. From such a point of view the author analyzes the various explanations of flight of ideas which have been offered by others. Well presented cases offer the material for this interesting discussion, which is written in a style that does not make for easy reading.

A Guide for Developing Psychiatric Social Work in State Hospitals. By Hester B. Crutcher. Price, 50 cents. Pp. 57. Utica, N. Y.: State Hospitals Press, 1933.

This book should prove its value as a manual for use in state hospitals. Miss Crutcher's treatment of the subject shows nice discrimination in the recommended use of a differentiated approach by the case worker in selected cases and ways in which to facilitate the routine services for all cases to keep the mechanics of admission, study, discharge and parole running smoothly. Though she includes numerous outlines as guides for different types of interview, she agrees with Dr. Goodwin B. Watson's concept that "the interview is a joint quest, not an inquisition nor imposition . . . an interview is starting a process." For those who are out of touch with social work in state hospitals, the service as the author visualizes it is a far cry from the taking of histories and carrying out of errands assigned to social workers in former times.

News and Comment

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

The fifteenth annual meeting of the Association for Research in Nervous and Mental Disease will be held at the Hotel Commodore, Forty-Second Street and Lexington Avenue, New York, on Thursday and Friday, Dec. 27 and 28, 1934. The meeting will consist, as usual, of morning and afternoon sessions, the morning sessions to begin at 9 a. m. and the afternoon sessions at 2 p. m.

The following program has been arranged:

Morning Session, Dec. 27

Peripheral Nerves and Sensory Nerve Endings.

A. Number, Size and Myelination of the Sensory Fibers in the Cerebrospinal Nerves. S. W. RANSON, M.D., Chicago.

B. Conduction in Nerves in Relation to Fiber Types. H. S. GASSER, M.D., New York.

C. The Mechanism of Sensory End-Organs. D. W. BRONK, M.D., Philadelphia.

D. Methods of Investigation of Sensation of Man and Theoretical Value of Results Obtained. H. C. BAZETT, M.D., Philadelphia.

1. Application to Problems of Cutaneous Innervation and Sensation. L. M. THOMPSON, M.D., Berkeley-San Francisco.
   AUTHOR: Does Dr. Thompson reside in Berkeley or in San Francisco?

Afternoon Session, Dec. 27

Visceral Sensations.

A. The Anatomic Relations of the Sympathetic System to Visceral Sensation. J. C. HINSEY, PH.D., San Francisco.

B. Cardiovascular Sensation. J. C. WHITE, M.D., Boston.

C. Visceral Sensation and Referred Pain. L. J. POLLOCK, M.D., and L. Davis, Chicago.

D. The Mechanism of Painful Sensations. P. HEINBECKER, M.D., and G. H. BISHOP, PH.D., St. Louis.

E. The Source of Visceral Impulses. C. H. FRAZIER, M.D.; J. W. WATTS, M.D., and C. A. W. UHLE, M.D., Philadelphia.

Morning Session, Dec. 28

Sensory Tracts and Mechanisms in the Cord and Brain.

A. Development of the Sensory System with Reference to the Local Sign. G. E. COGHILL, PH.D., and A. W. ANGULO Y GONZALES, PH.D., Philadelphia.

B. Central Levels of Sensory Integration. J. G. DUSSER de BARENNE, M.D., New Haven, Conn.

C. The Effects of Postcentral and Precentral Lesions on the Performance of Monkeys Trained to Discriminate Between Weights of Different Magnitude. T. C. RUCH, M.D., and J. F. FULTON, M.D., New Haven, Conn.

D. Studies of the Sensory Disturbances Resulting from the Excision of the Cerebral Cortex in Man. J. P. EVANS, M.D., and N. PETERSON, M.D., Montreal, Canada.

E. Summary of Clinical and Anatomic Findings Following Lesions in the Dorsal Column System in Macacus Rhesus Monkeys. A. FERRARO, M.D., New York.

Afternoon Session, Dec. 28

Clinical Cases Illustrating the General Principles and Mechanisms Developed in the First Three Sessions.

A. A Contribution to the Mechanism of Intracranial Pain. W. G. PENFIELD, M.D., Montreal, Canada.

B. Experimental Study of Cutaneous Innervation. I. H. LANIER, PH.D., New Orleans.

C. Hyperaffectivity and Other Subjective Sensory Disturbances. C. DAVISON, M.D., New York.

D. The Disturbances of the Time Relation to Sensitivity in Major Trigeminal Neuralgia. H. F. LEWY, M. D., Philadelphia.

E. Summary. FREDERICK TILNEY, M.D., New York.

A REGISTRY OF TUMORS OF THE BRAIN

A series of about two thousand tumors of the central nervous system collected by Dr. Harvey Cushing during his period of service at the Johns Hopkins Hospital and the Peter Bent Brigham Hospital has been brought to the Yale School of Medicine, New Haven, and put under the curatorship of Dr. Louise Eisenhardt. It is intended that these elaborately catalogued specimens should, so far as possible, be made useful to those interested in the subject, and it is hoped that the collection will be added to from many sources.

There are many problems relating to the classification of tumors and expectancy of life after the removal of a tumor that are as yet unsolved. Hence this series of cases may be of help to those who may encounter rare tumors that they may wish to have identified, if possible, and concerning which they may desire information, particularly on the basis of prognosis according to type.

Any one who may feel inclined to send specimens for diagnosis or to seek other information is welcome to do so. The following persons, several of whom are already familiar with much of the material, have consented to act as an advisory board: Dr. Percival Bailey, University of Chicago; Dr. F. C. Grant, University of Pennsylvania; Dr. S. C. Harvey, Yale University; Dr. G. J. Heuer, Cornell University; Dr. Wilder G. Penfield, McGill University; Dr. Ernest Sachs, Washington University; Dr. W. P. Van Wagenen, University of Rochester, and Dr. S. B. Wolbach, Harvard University.

LOUISE EISENHARDT, M.D., New Haven Hospital, New Haven, Conn.

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